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TROPICAL DISEASES BULLETIN

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Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1
(Telephone: MUSEUM 3041)

COMMONWEALTH MYCOLOGICAL INSTITUTE
5 APR. 1948

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BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES BULLETIN

Vol. 45] 1948 [No. 2

AVOIDABLE MENINGITIS

MEMORANDUM DRAWN UP BY THE PUBLIC HEALTH LABORATORY SERVICE AND THE LONDON SECTOR PATHOLOGISTS' COMMITTEE *

Every operative procedure entails some risk to the patient, but in simple operations like spinal puncture the risk ought to be practically negligible. The occurrence of meningitis following the withdrawal of cerebrospinal fluid or the administration of a spinal anaesthetic is a grave reflection on the methods used in many hospitals, because these "accidents" can be avoided by the adoption of a simple and reliable technique. That such a technique is not in fact universally employed is attested by the number of cases of avoidable meningitis reported in the literature during the past few years. Furthermore, as Garrod (1946) points out, "There is a natural reluctance to publish anything which may appear discreditable. . . . It is therefore probable that meningitis following spinal anaesthesia has been far commoner than the literature of the subject would suggest." This statement is endorsed by surgeons and anaesthetists whenever the subject comes up for discussion.

Nature and Sources of Infection

This memorandum is not concerned with meningitis secondary to some primary infective focus already present in the patient at the time of operation. It refers solely to meningitis that results from the direct inoculation of micro-organisms into the spinal canal. The organisms most frequently incriminated are *Ps. pyocyanea* and related organisms which can multiply in water at room temperature; less frequently staphylococci and other skin contaminants may be responsible. Some of the water bacteria fail to grow in ordinary culture media incubated at 37°C.; hence many cases have been diagnosed as irritative or aseptic meningitis which were probably the result of bacterial infection of the meninges. Organisms normally regarded as non-pathogenic may produce infection if they gain access to the very susceptible meninges.

The *sources* of contamination may be listed as follows :—

(1) Apparatus inefficiently sterilized or contaminated during use.
(2) "Sterile" water or saline used to rinse the apparatus.
(3) Hands of operator and assistants.
(4) Skin of patient.
(5) Anaesthetic, antibiotic or other solutions.

[* This memorandum supplements the recommendations of the Medical Research Council in their report (War Memorandum No. 15) on "The Sterilization, Use and Care of Syringes" (see this *Bulletin* 1945, v. 42, 843). Certain minor changes in the wording of two sentences have been made, with permission, in view of the special interests of readers of this *Bulletin*. *Ed.*]

Preventive Measures

The ideal would be to adopt the full aseptic ritual of a surgical operation for every spinal puncture. In many cases the time and place render this impossible. The following recommendations are therefore offered, not necessarily as ideal procedures but as practical methods applicable in nearly all circumstances.

(1) *Apparatus.*—If facilities are available, all apparatus including manometer should be enclosed within suitable containers and sterilized either by autoclaving at 15 to 20 lb. pressure for 20 minutes or by dry heat at 160°C. for an hour. The complete outfit can then be held ready for use at any time. If dry heat is used, the rubber tubing of the manometer should be sterilized by boiling. For syringes and needles dry heat is preferable but ordinarily necessitates the use of all-glass syringes. (Glass syringes with metal nozzles, which will withstand dry heat at 160°C. for 2 hours are now being manufactured.) Full details of these methods, together with recommendations for a hospital syringe service, are given in the Medical Research Council's War Memorandum No. 15 (1945) on " The Sterilization, Use and Care of Syringes ".

If autoclaving or dry heat sterilization cannot be employed, all apparatus should be sterilized immediately before the operation by boiling for 5 minutes, preferably in distilled water. A sterilizer with a perforated lift-up tray should be used ; at the end of boiling the tray is removed, placed in the inverted lid, covered with a sterile towel and left to cool.

In the occasional emergency which may arise in the patient's home a perfectly clean saucepan with a lid may be used. After boiling, the water should be drained off and the saucepan left with the lid on until cool. Methods of chemical disinfection such as soaking in spirit should *not* be used.

(2) *" Sterile " Water and Saline.*—These probably constitute the greatest source of danger. Hospital supplies are frequently contaminated either from inadequate sterilization initially or from contamination during previous use (SMITH and SMITH, 1941). Thus the Winchester bottle of " sterile " distilled water or saline, used repeatedly until empty, has frequently been incriminated as the source of water bacteria found in contaminated or infected cerebrospinal fluid. *If apparatus is sterilized as recommended above, rinsing and cooling solutions become quite unnecessary and their use should be abandoned.*

(3) *Hands of Operator.*—The operator should scrub up as for a major operation, or alternatively should don dry sterile surgical gloves. When gloves are not available it is important that his hands be dry before he handles any apparatus ; this may be accomplished by rinsing with industrial spirit and/or drying with a sterile towel. Where needle and syringe have to be assembled, the needle should be handled with sterile forceps. From this point onwards the operator should touch nothing except the sterile instruments and the skin of the patient until the operation is finished. The trocar when withdrawn should be laid on a sterile towel ; otherwise it may infect the spinal fluid if it is introduced again to clear the needle.

(4) *Skin of Patient.*—Thorough washing with soap and warm water followed by thorough, not perfunctory, swabbing with tincture of iodine or 70–90 per cent. alcohol will leave little risk of contamination of the needle by the patient's skin. The area treated should be the entire area exposed and the skin should be quite dry before puncture is made.

(5) *Anaesthetic and Antibiotic Solutions.*—No cases of meningitis have been traced to the presence of bacteria in anaesthetic solutions contained in sealed glass ampoules. Such ampoules are preferable to rubber-capped bottles intended for repeated use.

The sterilization of the outer surface of an ampoule is difficult and attended with such pitfalls that it is better not to attempt it. The ampoule should be

opened, after swabbing the neck with 70 per cent. alcohol applied with sterile swabs, by an assistant whose hands have been scrubbed and dried. It may be held in a sterile towel or piece of sterile lint. The operator must then introduce the needle of the syringe into the ampoule without fouling the mouth.

Other forms of container should be avoided except where absolutely necessary. If a rubber-capped bottle has to be used, it should be held in a sterile towel by the assistant, and the cap should be thoroughly swabbed with 70 per cent. alcohol or tincture of iodine. It is unwise to use rubber-capped bottles for more than a short time, and they should be replaced frequently, or, if the contents permit, returned to the central sterilizing depot each day for complete sterilization by an appropriate method.

The intrathecal injection of antibiotics such as penicillin and streptomycin demands the same high standard of aseptic technique ; and all precautions should be taken to ensure that the solutions themselves are sterile.

Reporting of Cases

The general adoption of the measures recommended here would, without doubt, reduce the incidence of " accidental " meningitis but would not close every possible loophole for infection. Further safeguards can be found only if cases are thoroughly investigated as and when they occur and with the employment of specialized bacteriological methods. The Public Health Laboratory Service will willingly co-operate with the hospital pathologist or other officer in carrying out such investigations as are required.

Gratitude is expressed to Sir Hugh Cairns and Professor Wilson Smith for the help they gave in the preparation of this memorandum.

REFERENCES

GARROD, L. P. (1946) *Brit. Med. Bull.*, v. 4, 106.
Medical Research Council War Memorandum No. 15. H.M. Stationery Office, 1945.
SMITH, W. & SMITH, Muriel M. (1941) *Lancet*, Dec. 27, 783.

SUMMARY OF RECENT ABSTRACTS*

II. YELLOW FEVER

General

CECCALDI (p. 75) reports that a small experiment suggested that penicillin may have some slight virucidal action on the yellow fever virus.

PERLOWAGORA and HUGHES (p. 657) discuss a complement-fixation test for yellow fever, in which they have used the globulin fraction of a mouse-brain antigen. This test becomes positive after even mild attacks of yellow fever, but rarely after vaccination with 17D ; it should prove useful in epidemiological studies, for tracing comparatively recent cases of yellow fever.

Epidemiology : Epizoology : Transmission

MAHAFFY *et al.* (p. 72) have brought together the results of mouse-protection tests performed on sera from various parts of East Africa, which have helped to define the areas in which yellow fever has occurred recently. These areas extend from the Belgian Congo to the Sudan and Eritrea, as far south as Northern Rhodesia, over a far wider area than would be suspected on the

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1947, v. 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

evidence of clinical diagnosis. The authors point out the important fact that a high proportion of cases in Africans are mild, and that mild yellow fever cannot be diagnosed clinically.

HADDOW *et al.* (p. 992) state that continuous studies made in Uganda have shown that, of the many groups of animals investigated, yellow fever immunity is found only in monkeys. The important species in this respect are *Cercopithecus nictitans mpangae* and *Colobus polykomos uellensis*. The species of mosquitoes chiefly suspected of transmission from monkey to monkey are mainly arboreal, and investigations indicate that *Aëdes africanus* may be the principal vector in this animal community. It seems likely that the *Colobus* monkeys are the chief species involved in the monkey-to-monkey cycle in uninhabited forest areas, but that the *Cercopithecus* monkeys are important in bringing the virus into contact with man. SMITHBURN and HADDOW (p. 71) have found yellow fever virus in wild-caught *Aëdes simpsoni*, and in *Aëdes* of other species (excluding *aegypti*) in Western Uganda. They give reasons for thinking that *Aëdes africanus* may be implicated. There is apparently an extra-human cycle of yellow fever in monkeys and mosquitoes in the Semliki forest. HADDOW *et al.* (p. 516) have investigated the vertical distribution and the biting cycle of mosquitoes in an area of rain-forest in Uganda. Catches were made up to 80 feet from the ground, and the mosquitoes caught were identified, pooled, and injected into monkeys to test for yellow fever virus. This was found in only one batch of *Aëdes* species, containing, among others, *Aëdes africanus*, a known potential vector. *Aëdes africanus* is the commonest arboreal culicine, and is most abundant 50–60 feet from the ground. In the area studied the monkey population is about 400 to the square mile. The authors give much information on temperature and humidity, and on the biting-times of the various mosquitoes. They note that *Anopheles gambiae* is by far the commonest mosquito, even far from human haunts.

BAILEY (p. 657) reports a study of the sylvan mosquitoes of Gede, a settlement in forest country on the coast of Kenya. *Aëdes* species haunt the upper forest strata.

LEWIS (p. 656) gives much general information on mosquitoes of the Sudan, in relation to yellow fever, and includes a list of the known vectors; but the paper cannot satisfactorily be abstracted further. Mosquito control in the Sudan has rendered impossible an urban epidemic transmitted by *Aëdes aegypti*, and has eliminated this mosquito from the river steamers.

DURIEUX *et al.* (p. 991) found protective antibodies in 88 per cent. of a series of baboons (and one other monkey) in French territory near the Gambia. They note that the percentage usually recorded is of the order of 20–25 per cent., and they make the point that further investigation indicated that the positive results could not be explained by the presence of non-specific substances in the sera. Wild animals are evidently important as reservoirs in this part of Africa.

TAYLOR *et al.* (p. 414) undertook an extensive investigation in the State of Bahia, Brazil, in which they found evidence of jungle yellow fever spreading to man in the absence of *Aëdes aegypti*. Positive neutralization tests were found in man, most commonly in adult males who frequently visited those forests which are more than 75 years old. Many mammals and mosquitoes were collected and tested, but although protective bodies (which were probably not specific) were found in certain rodents, the only definite evidence of transmission was in relation to marmosets (of which four *Callithrix penicillata* were found with circulating virus) and *Haemagogus spegazzinii* (from which virus was obtained). There is, therefore, a close relationship between immunity in man and marmosets, the prevalence of *Haemagogus* species, and the older climax type of tropical rain-forest. WADDELL and TAYLOR (p. 309) think that the marmosets *Leontocebus chrysomelas* and *Callithrix penicillata* are the principal,

if not the sole, vertebrate hosts of the yellow fever virus in part of the State of Bahia, Brazil.

BATES and ROCA-GARCIA (p. 310) think that the opossums *Metachirus* and *Caluromys* are the two most susceptible Colombian marsupials, but even with these, infection of *Haemagogus* mosquitoes is difficult, so that it is doubtful if the local marsupials are important in the *Haemagogus* cycles in nature. On the other hand, the cycle was easy to maintain with certain monkeys and marmosets [but see below]. ANDERSON and ROCA-GARCIA (p. 992) show that the opossum *Caluromys laniger* is susceptible to infection with yellow fever virus, although the infection is not fatal. After injection of virus, in most cases the virus circulates in the blood for several days, and specific neutralizing antibodies appear later. Some of the animals maintain the neutralizing antibodies, but in others the antibodies decrease and may disappear, in which case the animal may once more become susceptible to infection. Certain anomalies were found in a proportion of the animals, in relation to infection and immunity, but the majority reacted as described.

ANDERSON and OSORNO-MESA (p. 309) note that other workers have shown that *Haemagogus spegazzinii falco* and *H. equinus* are capable of transmitting yellow fever virus, and report that they themselves have proved *H. splendens* also to be capable of transmitting the virus under laboratory conditions. BATES and ROCA-GARCIA (p. 308) have noted that *Haemagogus* mosquitoes fed on Saimiri monkeys infected with a pantropic strain of yellow fever virus rarely become infected themselves, and in a series of experiments with French neurotropic virus passaged in Saimiri monkeys, they failed to demonstrate infection in any of the *Haemagogus* mosquitoes subsequently fed on them.

In a study of the infection of *Haemagogus* mosquitoes with yellow fever virus, the same authors (p. 415) have shown that the virus diminishes in amount in the mosquitoes for a few days after ingestion, and may even die out altogether, but that multiplication then takes place very slowly, and the mosquito may become infective by bite 10–28 days after infection. These processes depend very largely on the environmental temperature, and the temperature range found in nature in the haunts of *Haemagogus* species not only favours the development of the mosquitoes, but also of the virus in them.

SNIJDERS *et al.* (p. 993) report on protection tests carried out in Surinam, where they indicate the presence of jungle yellow fever.

KOPROWSKI (p. 580) comments on the fact that the sera of various animals have shown virucidal properties against the yellow fever virus, even though the animals have never been infected. He shows that many of these sera are virucidal also to certain other viruses which are not found in the countries concerned. This non-specific virucidal property is transitory, and the animals concerned react specifically to injection of yellow fever virus.

Vaccination

FOX (p. 1062) has studied the factors which influence the multiplication of virus 17D in tissue cultures, but details of his findings must be sought in the original. FOX and LAEMMERT (p. 1062) report observations on the infection of developing chick embryos, but these again must be sought in the original. They make the point that prolonged embryo-to-embryo passage of strain 17D, and the French neurotropic strains, did not reveal significant changes in the character of the virus. It is still unknown by what means the attenuated variants of yellow fever virus (such as 17D) may be produced ; continuous embryo passage usually fails to produce them.

BURRUSS and HARGETT (p. 994) have found that 17D vaccine virus may be desiccated at room temperature without more loss than occurs at lower temperatures, but they advise that it should then be stored at −20°C. to −25°C.

Adequately desiccated vaccines may remain potent enough for use even if kept at tropical temperatures for a few weeks, but great loss of virus does take place under these conditions. When the vaccine is diluted for use, 1 : 1 or 1 : 10 dilutions should be used within one hour, and 1 : 100 within 10 minutes.

PELTIER (p. 417) describes the preparation of the dry mouse-brain vaccine made in Dakar. The brains of mice which have been inoculated intracerebrally, and which show paralysis, are desiccated, ground with an inert powder, and kept at —4°C., to be reconstituted, for scarification, with a gum solution. This vaccine is sometimes mixed with smallpox vaccine. LAIGRET (p. 580) does not approve of the mixing of smallpox and yellow fever vaccines, for scarification, because he believes that the neurotropic properties of each may thus be enhanced.

In the *Epidemiological Information Bulletin* (UNRRA Health Division) (p. 73) there is a detailed account of a series of comparative tests of the neurotropic brain vaccine made at Dakar, and administered by scarification, in a gum solution, with or without smallpox vaccine, and of the American 17D vaccine given subcutaneously. The Dakar vaccine was undoubtedly a potent immunizing agent, producing neutralizing antibodies in the serum of practically 100 per cent. of the subjects tested. But vaccine 17D also produced neutralizing antibodies in practically 100 per cent., and it has shown itself to be a powerful immunizing agent in the field; 17D does not produce encephalitis, which has been reported after the use of mouse-passage neurotropic vaccine used without immune serum. Each of these vaccines is unstable at temperatures above 5°C., but can be kept for long periods if dried and frozen. In a long comment on this paper, MACCALLUM discusses the history of yellow fever vaccination. The intraperitoneal mouse-protection test appears to be more sensitive than the intracerebral test, in detecting neutralizing antibodies.

ANDERSON and GAST-GALVIS (p. 813) have investigated the state of immunity of people vaccinated about 5 years previously, in Colombia. They found evidence of neutralizing antibodies in some 93 per cent., and show that there is no essential difference in response between children and adults. They conclude that revaccination is not usually necessary within 5 years of vaccination with 17D.

Control

FINDLAY (p. 579) discusses the spread of yellow fever and other diseases by aircraft, and suggests that an international organization should be formed under the W.H.O., to control airfields, disinsectization of aircraft, yellow fever vaccine, and vaccination certificates.

DE CAIRES (p. 658) reports on the yellow fever service of British Guiana. He considers that DDT is one of the very important means of controlling *Aëdes aegypti*, but that much investigation remains to be done, for instance, in relation to the ability of eggs of this mosquito to remain viable for long periods in dry conditions. In a later report (p. 994) he states that this service has now ceased to exist as a separate organization, having become part of the mosquito control service. The value of DDT is again emphasized, but control depends chiefly on a high standard of efficiency in all branches of the service, which has been attained. No case of yellow fever was reported in the Colony during 1946.

Charles Wilcocks

MALARIA

BLACKIE, W. K. **Malaria, with special reference to the African Forms.**
This book is reviewed on p. 216.

ASCOLI, Maurizio. Nuove vedute sulla malaria. Studi di Medicina e Biologia. [**New Outlook on Malaria.**] 211 pp., 24 illustrations. 1946. Rome: Istituto Bibliografico Italiana. [*L.* 350.]

This volume contains papers contributed to a Conference on Malaria convened in Palermo. The first part (119 pages) deals with the rationale, application and results of the adrenaline treatment of malaria, with which the name of Ascoli is so closely associated. There are 12 papers written by Professor Ascoli and ten of his collaborators, dealing with all aspects of the question. Account is taken of the extensive literature concerning this method of treatment that has appeared during the last fifteen years; 191 references are listed. This very complete exposition of the subject is deductive.

The second part of the volume contains a paper by G. BUONOMINI outlining modern conceptions of the cycles of development of malaria parasites in vertebrate hosts. The same author with M. MARIANI contributes a paper on the races of *Anopheles maculipennis* and anophelism without malaria in Europe. G. D'ALESSANDRO and M. GRACOLICI deal with the suppressive use of anti-malarial drugs. M. ASCOLI and S. SORCE describe an ingenious method of concentrating malaria parasites in blood examinations by centrifuging citrated blood. *Norman White*

ZOTTA, G., RADACOVICI, E., TEODORESCU, A. M., GEORGESCU, M., MARDARE, I., DUPORT, M., ATANASIU, M. & TRIFON, A. Evoluţia endemiei palustre in judeţul Teleorman. [**The Course of a Malaria Epidemic in Teleorman.**] *Rev. Stiinţelor Med.* Bucharest. 1946, Sept.–Dec., v. 36, Nos. 9/12, 781–815, 9 graphs & 1 map. French summary.

Teleorman is on the left bank of the Danube: between 1935 and 1942, there was an epidemic of malaria, in two phases; the first (1935–1938) was of moderate intensity and constant extent; the second (1939–1942) was more severe.

In general, cases were seen mostly in river valleys and particularly those of the rivers Urluiu, Calmatzuiu and Teleorman, in the lower parts of which the flood areas of the Danube may also be included.

The serious nature of the epidemic during the war years may be attributed, not only to war conditions, but to natural factors and also to man-made causes, particularly that of rice cultivation which was a recent introduction. All along the rivers, the local inhabitants had constructed dams, which resulted in the formation of breeding places for mosquitoes.

All human species of *Plasmodium* were found, except *P. ovale*; the proportions varied each year. In general, *P. vivax* infections were commoner than those caused by *P. falciparum*, except in 1936 (*P. vivax* 624; *P. falciparum* 772) and 1939, when the numbers were about equal (1,373 and 1,334). Quartan was rarely seen, and in 1939 was not reported at all.

Although all varieties occurred together throughout the year, each showed a definite seasonal period of spread; *P. vivax* was prominent in spring and summer, *P. falciparum* at the end of summer and throughout the autumn, and *P. malariae* in the colder months.

All types of *Anopheles maculipennis* found in Rumania, on the left bank of the Danube, constituted insect vectors, namely *A. m. messae*, *A. m. atroparvus*

and *A. m. maculipennis*. The first-named occurs in the southern flood-region where stagnant water is in evidence : its rôle as a malaria vector is important, though not striking.

A. m. atroparvus is found throughout the Department wherever the soil is salty and the water covering it becomes brackish : it plays a predominant part in transmission throughout the year.

A. m. maculipennis is predominant in the northern half of the Department. While it is not in general regarded as a vector, it must be suspected to play an important rôle among a population who are so much exposed to it outdoors where they sleep in the summer, without providing themselves with any protection against it. *H. J. O'D. Burke-Gaffney*

SIPPE, G. & TWINING, May: **Survey and Field Treatment of Malaria in Mauritius.** pp. v+76, 50 figs. & 5 pls. 1946. Published on behalf of the Government of Mauritius by the Crown Agents for the Colonies. London : 4 Millbank, S.W.1. [25/- or *Rs.* 16.67.]

This is the most comprehensive survey of malaria in Mauritius yet published. The survey was undertaken at the request of the Military Authorities when it became necessary, in 1942, to post troops and labour gangs in certain of the coastal areas where malaria was rife. The detailed work of the survey was carried out by three V.A.D. assistants and three male laboratory assistants. In assessing the incidence of the disease, children from two to ten years of age were examined. To study the development of immunity, babies from birth to two years of age and persons from eleven to twenty years of age were examined.

Mauritius is an island of volcanic origin, 700 square miles in extent with a high central plateau. In the north and south-east there are large areas below the 600-feet level ; elsewhere the coastal plain is narrow. At high altitudes the annual rainfall exceeds 150 inches. There are numerous small rivers and streams, and irrigation canals for sugar cane. In the coastal belt the drainage is poor. The population is about 400,000 (600 to the square mile) 70 per cent. of whom are Indians.

Malaria-carrying mosquitoes were introduced into Mauritius in 1865, either from Madagascar or from East Africa. The result was devastating. In 1866, the death-rate for the whole island was 32·1 per thousand ; in 1867, it rose to 120·5 per thousand. It was, however, not until 1869 that the disease completely encircled the island. Since then malaria has been very largely confined to the coastal belt. It was so when Ronald Ross made his survey in 1908. Small outbreaks of great intensity have occurred, however, from time to time at higher altitudes. Thus at Alma, 1,500 feet, a severe outbreak occurred during the first quarter of 1943 when a thousand cases were notified in a camp with a strength of 1,200 ; the spleen rate was 90 per cent.

The two malaria vectors are *A. gambiae* and *A. funestus*. *A. maculipalpis* is only occasionally found. *A. mauritianus* [*A. coustani*] has not been shown to be a vector.

The average spleen rate of children living below 600 feet was 46 per cent. ; from 600 to 1,200 feet, 13 ; from 1,200 to 1,800 feet 8 (excluding Alma, on the occasion mentioned above) ; above 1,800 feet 7. Fifty-nine per cent. of the population live below 600 feet, this area constituting a little more than half the total area of the island.

Below 600 feet, the average parasite index was 36 per cent. (*P. falciparum* 48, *P. vivax* 35, *P. malariae* 32, mixed infections 14 per cent.). Above 600 feet, the parasite index was 12 per cent. (*P. falciparum* 40, *P. vivax* 43, *P. malariae* 21, mixed infections 16 per cent.).

Temperature appears to be the limiting factor in malaria transmission ; there is but little transmission even at sea level in the winter. The breeding of *A. gambiae* may, however, occur as high as 1,500 feet when conditions are particularly suitable. The malaria "season" extends from December or January to the beginning of June.

A large proportion of the Mauritius population have a very poor nutritional standard ; this probably accounts in part for failure to develop immunity. The maximum spleen rate in hyperendemic areas is reached at the age of five ; very little reduction in spleen rate and no reduction in spleen size is seen even up to the age of 20. The parasite rate shows a very rapid rise to the age of four ; thereafter there is a gradual decline. By the age of 14 it has fallen to half. The gametocyte rate curve corresponds with the parasite rate curve. Children between one and eight are the main danger to the community.

An interesting part of the report deals with the relationship between malaria and malnutrition. In villages with spleen rates below 20 per cent., nutrition was unsatisfactory in 2·4 per cent. of children and borderline in 11·9 per cent. In villages with spleen rates above 20 per cent., nutrition was unsatisfactory in 6·8 per cent. of children and borderline in 20·3. The commonest signs of malnutrition were mosaic skin, angular stomatitis and glossitis, and anaemia of the macrocytic type: Thirty per cent. of children with enlarged spleens showed macrocytosis.

In the Black River District, where nearly all villages have spleen rates of 90 per cent. or over, the infant mortality rate was 303 per 1,000 live births. In the Plaines Wilhems District, parts of which are almost malaria-free, the infant mortality rate was 114 per thousand.

As an emergency measure, children living in proximity to military areas were treated by a combination of drug therapy or extra feeding or both. When transmission was not excessive and nutrition was satisfactory, adequate control was secured with either quinine or atebrin [mepacrine]. Supplementary feeding with milk markedly increased the efficacy of drug treatment. Shark liver oil and yeast were also of value. Vegetable soup and yeast alone were both ineffective. *Norman White*

SAUNDERS, G. M. & SCOTT, V. **Preservation of *Plasmodium vivax* by Freezing.** *Science.* 1947, Sept. 26, 300–301.

Protozoa, unlike viruses, are difficult to preserve for long periods in an unchanged condition. Low temperature freezing, however, has been successfully employed up to 70 days in the case of animal plasmodia. The authors use such a method for the preservation of *Plasmodium vivax*. The infected blood is taken into 4 per cent. sodium citrate solution, in the proportion of 20 parts blood to 3 parts citrate. About 2–3 cc. of the citrated blood are put into small, plastic, screw-capped vials and the blood is rapidly frozen at a temperature of —75°C. by immersion in a mixture of alcohol and dry ice, then stored in a dry-ice box at –50°C. Before use, the blood is thawed in a water-bath at a temperature of 40°–42°C. In this way, parasites remain viable up to 15 days or more and, in one case, up to 37 days.

The results indicate some modification from the normal in the ensuing infection, including, in at least one of 3 cases, a mild chill after inoculation ; however, changes are only to be expected when it is considered that freezing and thawing cause almost complete haemolysis of the red blood cells and considerable modification in the staining reactions and morphology of the parasites. *P. C. C. Garnham*

MOSNA, E. Un nuovo metodo di produzione in vitro del processo di flagellazione dei microgametociti dei parassiti malarigeni. [**Flagellation of Microgametocytes of Malaria Parasites** *in vitro*.] *Riv. di Parassit.* Rome. 1947, Mar., v. 8, No. 1, 63–5.

Two or three drops of blood are removed from the comb or from a vein of the wing of a fowl infected with *Plasmodium gallinaceum* on to a slide and mixed with an equal quantity of a 3 per cent. solution of citrate of sodium. By rocking the slide, a homogeneous mixture is obtained. A very thin cover glass is placed on the mixture in such a manner that no pressure is applied. On examining the preparation microscopically it will be noted that the red cells arrange themselves in a floral design, the centre of which will be found to be a flagellating microgametocyte. The observations were repeated with human blood containing *P. vivax*, but the floral arrangement was not so marked as in the case of fowl's blood. As a modification of the method, the blood can be taken into a syringe containing the citrate solution and the mixture run on to the slide for observation. *C. M. Wenyon*

PAL, R. **Marking Mosquitoes with Fluorescent Compounds and Watching them by Ultra-Violet Light.** [Correspondence.] *Nature.* 1947, Aug. 30, 298–9.

The author has shown that mosquitoes (*Anopheles maculipennis* var. *atroparvus*, *Culex molestus* and *Aëdes aegypti*) are not adversely affected by ultra-violet light, that they can take up enough fluorescent dust (anthracene and other substances) on their bodies to enable them to be observed at a distance of 10 feet in ultra-violet light, and that they are not adversely affected by the dust. Observations are therefore possible on the behaviour of mosquitoes at night, which could not otherwise be made. *Charles Wilcocks*

CHELĂRESCU, M. & CURPAN, C. Varietăţile de *A. maculipennis* din regiunea sibiu, judetul sibiu. (Lucrare făcută sub conducerea Prof. M. CIUCA şi Prof. L. BALLIF). [**Types of** *Anopheles maculipennis* **in the Sibiu Region (Rumania).**] *Rev. Ştiinţelor Med.* Bucharest. 1947, Jan.–Apr., v. 36, Nos. 1/4, 63–75. French summary (8 lines).

Studies made in August 1944 in a malaria-free area of the Sibiu region showed the following prevalence of anophelines : *Anopheles maculipennis maculipennis* 63·3 per cent. ; *A. m. messae* 31·9 per cent. ; *A. m. atroparvus* 2·7 per cent. Examination of eggs also demonstrated the occasional presence of eggs having a different external configuration.

The first two species, when infected experimentally, proved to be more resistant than homologous species from a hilly area (Socola-Iaşi).

H. J. O'D. Burke-Gaffney

UNGUREANU, E. & SHUTE, P. G. **The Value of the Wing Scales as an Aid to the Taxonomy of Adult** *Anopheles maculipennis*. *Proc. Roy. Entom. Soc.* London. Ser. B. 1947, Aug. 15, v. 16, Pts. 7–8, 79–85, 1 pl. [10 refs.]

A paper by Ungureanu (1944) on the wing scales of the *Anopheles maculipennis* complex has already been noticed [this *Bulletin*, 1947, v. 44, 557]. The material on which the present studies were based was obtained from Rumania, England, Algeria, Holland and Italy ; the collection from Albania in the London School of Hygiene and Tropical Medicine was also examined.

From the accumulated data on shape and size of wing scales, the authors have been able to construct a key, which they claim is 90 per cent. accurate, for the identification of *A. maculipennis atroparvus*, *messeae*, *maculipennis* and

elutus (*sacharovi*). It is not yet possible to distinguish the larvae of these races except *elutus*; but keys are given for the separation of the eggs of the above and *labranchiae*, and for the identification of the males, the latter being based on details of the hypopygia.

In view of the biological and morphological facts now known, the authors consider that the *A. maculipennis* group consists of at least four species rather than of varieties; *A. labranchiae* is not included yet, because sufficient material has not been studied and it can only be separated from *atroparvus* on egg characters. The wing scales of *A. m. maculipennis*, *atroparvus* and *messae* are shown in a photograph. *H. S. Leeson*

MATTINGLY, P. F. **Notes on the Early Stages of certain Ethiopian Mosquitoes, with some Locality Records from British West Africa.** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 239–52, 4 figs. [20 refs.]

This paper contains a description of the larva and pupa of *Anopheles domicolus*, and some corrections and additions to existing descriptions of the pupae of *A. wilsoni*, *A. nili*, *A. hargreavesi*, *A. argenteolobatus* and *A. multicolor*. Some points of difference between the larvae and pupae of *A. turkhudi* and *A. hispaniola* are given and there is a note on the unreliability of the various criteria for distinguishing the larvae of *Aëdes grahami* from other members of the subgenus *Mucidus*.

The locality records include anophelines and culicines collected in British West Africa between September 1942 and December 1944, but do not include new records of anophelines already published by the author in 1944 [this *Bulletin*, 1945, v. 42, 434]. The present new distribution records are indicated in the concluding notes on species. *H. S. Leeson*

GELFAND, H. M. **Natural Malaria Infection in** *Anopheles rufipes* **(Gough).** *J. Trop. Med. & Hyg.* 1947, Aug., v. 50, No. 8, 159–60.

The author has found the type form of *Anopheles rufipes* infected at Kano, N. Nigeria, and states that previous dissections of small numbers had always been negative. Larvae were found only in large, sunlit, stagnant pools with clean water and upright, grassy vegetation, often along with *A. funestus* but never with *A. gambiae*.

A. rufipes may be found in human habitations at the end of the rainy season in N. Nigeria, but in relatively small numbers only; *A. funestus* especially, and *A. gambiae*, are much more numerous. Its importance as a vector of malaria is probably slight. *Charles Wilcocks*

RAO, V. V. **On Gonotrophic Discordance among certain Indian Anopheles.** *Indian J. Malariology.* 1947, Mar., v. 1, No. 1, 43–50. [11 refs.]

The author describes some preliminary work on *Anopheles annularis* and *A. culicifacies* to show that while in the autumn there is a certain amount of gonotrophic dissociation, there is no general suspension of sexual activity in any species *en masse*, but that some individuals among the Indian anophelines enter into a condition midway between gonotrophic dissociation and gonotrophic concordance. In a mosquito in this state, which he calls gonotrophic discordance, the development of the ovaries does not keep pace with the nutrition but is dependent on repeated feeding; full ovarian development may only be completed after a prolonged period, and during this time the female feels no urge to leave its feeding place to lay eggs. The author therefore puts forward the hypothesis that, as repeated feeding would appear to increase the chances of

infection, it is the mosquitoes with suspended or delayed sexual activity which may alone be responsible for malaria transmission, while the majority, which remain sexually active, do not as a rule transmit the disease, but help to keep up the population.

The author is unable to pursue the matter further, but hopes it will be investigated by other workers. *H. S. Leeson*

WHITE, R. Senior. **On the Anthropophilic Indices of some Anopheles found in East Central India.** *Indian J. Malariology.* 1947, Mar., v. 1, No. 1, 111–22. [21 refs.]

The results are tabulated of some thousands of precipitin tests on the stomach contents of sixteen species of *Anopheles* captured in East Central India. In the case of five of these species (*Anopheles culicifacies, fluviatilis, varuna, minimus,* and *annularis*) the results of dissections are also given in order that the infection rate may be compared with the anthropophilic index. The figures are presented under three heads: houses, cattlesheds and out-of-doors. The author suggests that the differences observed in tropisms and in vectorial capacity, point to the existence of biological races among these species, though only in the case of *A. varuna* has any evidence been recorded (egg measurements) which might support this view; these measurements are awaiting statistical analysis.

The information regarding the remaining eleven species is much less complete and no infection rates are given for comparison. *H. S. Leeson*

FERNÁNDEZ MELÉNDEZ, A. Aportación al estudio del *Anopheles vestitipennis* en Cuba. [**A Study of** *Anopheles vestitipennis* **in Cuba.**] *Tijeretazos sobre Malaria.* Venezuela. 1946, Sept., v. 10, No. 3, 133–6.

In Cuba, *A. vestitipennis* may be regarded as a much more important vector of malaria than was hitherto locally believed.

It shows a marked preference for feeding on human blood. *A. albimanus* shows no preference between human and animal blood, while *A. crucians* and *A. grabhami* possess definite zoophilic characteristics.

Dissections of the stomachs and salivary glands of *A. vestitipennis* gave negative results, indicating that malaria transmission by the species was not active during the course of these investigations.

H. J. O'D. Burke-Gaffney

GABALDON, A. & COVA-GARCIA, P. Zoogeografia de los anofelinos en Venezuela: III. Relaciones con el terreno y clima. [**Distribution of Anophelines in Venezuela: III. Meteorological Considerations.**] *Tijeretazos sobre Malaria.* Venezuela. 1946, Sept., v. 10, No. 3, 164–79.

BOYD, M. F. **A Review of Studies on Immunity to Vivax Malaria.** *J. National Malaria Soc.* 1947, Mar., v. 6, No. 1, 12–31, 13 figs. [10 refs.]

In this address, the author brings together the important observations made by him and his co-workers on immunity to *P. vivax* infections during a prolonged experience of malaria therapy. A clinical attack of three weeks or longer after inoculation with *P. vivax* indicates that the patient was previously completely susceptible. Short attacks from one day to two weeks may follow either heterologous or homologous reinoculation, indicating, in the latter case, that immunity is incomplete. Homologous reinoculation may be followed by no clinical attack or fail altogether; the latter indicates a very effective refractory condition. A comparison of the parasite density at the beginning and the end of the clinical attack shows that a tolerance to the presence of the

parasites is the first manifestation of developing immunity. Soon after the infection becomes latent, the host is able to destroy numbers of parasites enormously greater than the few which can initiate an infection in a susceptible person. This destructive mechanism does not seem to be operative against sporozoites, but the resulting trophozoites will quickly disappear. The state of complete refractoriness may be of considerable duration ; there is no evidence that its persistence is dependent upon the persistence of latent infection. The failure of serum of hyperimmune persons to confer passive immunity on susceptible persons indicates that the immunity is not humoral.

The possibility of conferring active immunity by inoculation with killed parasites is difficult to determine. Two susceptible patients, saturated with quinacrine, were each given three inoculations of living parasites, which were presumably killed *in vivo*. Subsequent reinoculation by infected mosquitoes was followed by only a short clinical attack in each case. *Norman White*

WHORTON, C. M., KIRSCHBAUM, W. R., PULLMAN, T. N., JONES, R., Jr., CRAIGE, B., Jr., ALVING, A. S., EICHELBERGER, Lillian & COULSTON, F. **The Chesson Strain of *Plasmodium vivax* Malaria. I. Factors influencing the Incubation Period.** *J. Infect. Dis.* 1947, May–June, v. 80, No. 3, 223–7. [15 refs.]

The Chesson strain of *P. vivax* is of New Guinea origin. The observations recorded concerned psychotic patients in a hospital, and volunteer inmates of a penitentiary. Of 121 individuals receiving trophozoite infections, heparinized whole blood, 66 were inoculated with compatible blood, 55 with incompatible blood. The mean incubation period of the former group was 2·1 days ; of the latter group 4·8 days. " Inoculation fever " is in most instances related to blood incompatibility. The incubation period varied inversely with the number of parasites in the inoculum.

In mosquito-induced infections there was a negative correlation between the approximate number of sporozoites injected and the length of the prepatent period. Three subjects who were bitten by from 45 to 80 heavily infected mosquitoes had prepatent periods of 9, 11 and 12 days as compared with the mean prepatent period of 13·6 days in 139 individuals each of whom was infected by the bites of 10 infected mosquitoes. *Norman White*

CRAIGE, B., Jr., ALVING, A. S., JONES, R., Jr., WHORTON, C. M., PULLMAN, T. N. & EICHELBERGER, Lillian. **The Chesson Strain of *Plasmodium vivax* Malaria. II. Relationship between Prepatent Period, Latent Period and Relapse Rate.** *J. Infect. Dis.* 1947, May–June, v. 80, No. 3, 228–36, 5 figs.

These observations were carried out in a non-endemic area ; only presumably susceptible white males were involved ; and observations were restricted to primary attacks and first or second relapses, which were promptly treated by a variety of drugs.

In persons infected with the Chesson strain of *P. vivax*, by the bites of 10 infected mosquitoes, the relapse rate was high when the prepatent period was short. Persons with a prepatent period of 14 days or less had a relapse rate of 96 per cent. after treatment of the primary attack. When the prepatent period was 15 days or more the relapse rate was 58 per cent. One hundred and eleven cases were studied. The relapse rate after treatment of the first relapse was 85 per cent. in patients who had had a short prepatent period, and 37 per cent. in those who had long prepatent periods (82 cases observed).

The duration of the first latent period after treatment of the primary attack was usually short if the prepatent period had been short ; 89 per cent. of such

patients relapsed within 30 days, whereas only 46 per cent. of the relapses that occurred after long prepatent periods did so within that 30 days.

When the preceding latent period was under 30 days the relapse rate after treatment of the attack was 85 per cent. whereas it was only 52 per cent. when the latent period had exceeded that period (109 observations). The length of succeeding latent periods was positively correlated to the length of preceding latent periods.

The 30-day dividing line is not applicable to patients who have been treated previously with atebrin or with other drugs that persist in the body.

The relative importance of virulence and immunity as factors determining the severity of infections cannot be evaluated in such studies as these. The number of sporozoites injected is an important factor. If this be very high, the prepatent period is usually short. *Norman White*

WHORTON, C. M., YOUNT, E., Jr., JONES, R., Jr., ALVING, A. S., PULLMAN, T. N., CRAIGE, B., Jr., & EICHELBERGER, Lillian. **The Chesson Strain of *Plasmodium vivax* Malaria. III. Clinical Aspects.** *J. Infect. Dis.* 1947, May–June, v. 80, No. 3, 237–49, 8 figs. [23 refs.]

This is a note of the clinical aspects of 195 sporozoite-induced and 125 trophozoite-induced cases of *P. vivax* malaria, Chesson strain. There were very few prodromata. Irregular remittent fever was observed during the first few days in both types of infection. In sporozoite infections, 80 per cent. of patients with primary attacks had quotidian fever; the incidence of quotidian fever was lower in relapses. In trophozoite-induced infections early quotidian paroxysms usually changed to tertian as the disease regressed. Chills were not usually experienced during initial remittent fever. In general the signs and symptoms appear to have differed little, if at all, from those generally seen in *P. vivax* malaria. *Norman White*

COOPER, W. C., COATNEY, G. R. & RUHE, D. S. **Studies in Human Malaria. V. Homologous Strain Superinfection during Latency in Subjects with Sporozoite-induced Vivax Malaria (St. Elizabeth Strain).** *Amer. J. Hyg.* 1947, July, v. 46, No. 1, 141–8, 1 fig. [20 refs.]

Fifty million homologous-strain *P. vivax* parasites were injected intravenously into 15 patients, 4 months after their original infection with mosquitoes. The long-term latency in ten of these patients had resulted from complete suppression of early attacks by quinacrine [mepacrine] or NIH-204 (SN-1796). In the other five patients latency followed treatment of early attacks. All the recipients except one developed prompt and severe attacks of malaria as the result of this superinfection. Neither by prepatent periods, incubation periods, densities of parasitaemia at onset of fever, rates of increase of parasitaemia, peak parasite densities, fever peaks nor responses to therapy could any consistent difference be found between the quinacrine group, the NIH-204 group, the otherwise treated group or in two patients who had experienced no prior sporozoite-induced infection. The one failure to secure a definite superinfection was in a patient who exhibited persistent patent parasitaemia after an inadequately treated early relapse. Treatment of all superinfections was begun on the 11th day after inoculation. The patients who developed superinfections later developed delayed attacks apparently resulting from the original sporozoite infections. These late attacks were contemporaneous with those of fifteen other patients who had received sporozoite infections at the same time but had not had superinfections. *Norman White*

Ross, P. **Sub-Tertian (Malignant Tertian) Malaria in Europeans.** *East African Med. J.* 1947, Aug., v. 24, No. 8, 278–88.

The author has over 20 years' experience in treating subtertian malaria amongst Europeans in Kenya. Most of his service has been in the Kisumu and Mombasa districts, and he has treated over one-thousand patients in hospital and several thousands as out-patients.

He considers that the "protean" nature of subtertian malaria has been greatly exaggerated and that an acute attack is a clear-cut entity and is comparatively easily diagnosed. In a patient coming from a malarious district, having a temperature, where no antimalarial drug has been given, competent examination of the blood repeated at intervals of 12 to 24 hours will prove the presence or absence of the disease almost invariably. If such drug has been given, two courses are open: either the drug is continued in full doses for a week—failure to respond being almost certain evidence that the condition is not malaria—or it is stopped and repeated blood examinations are made (the ideal course). [This of course is safe only when the patient is under close observation.]

It is not believed that, under proper observation, harm ever results from delaying treatment, except in children. The author has never seen a case of coma or convulsions with a negative blood slide. The habit of necessarily ascribing all of a patient's symptoms to a subtertian infection found in the blood is a bad one, and moreover textbooks do not sufficiently discriminate in their descriptions of the disease as it affects Europeans, Asians and Africans. In Europeans, dysenteric symptoms due to malaria are thought to be very rare; and even if parasites are found, the stools should be carefully examined in such cases. [Malaria and amoebic dysentery not infrequently co-exist in certain districts.]

The author has found that the disease rarely simulates appendicitis, although he has met with a proved case in which an appendix abscess subsequently developed. Chronic subtertian malaria is considered usually to be the result of repeated reinfections and is met with in Europeans living in an area so malarious that reinfections are unavoidable. Such patients treat themselves with quinine or mepacrine (usually in quite inadequate doses and irregularly), get into a state of "uneasy equilibrium" and are prone to blackwater fever.

Finally, the ultimate diagnosis of malaria rests with the microscope.

The newcomer is advised that particular note should be taken of the district from which the patient comes. [Very sound advice in East Africa.]

Areas are divided into Group I, townships such as Kisumu and Mombasa, where residents are liable to occasional infections only, and Group II, hyperendemic areas where repeated reinfections are liable to take place. Care should be taken in ascribing unusual symptoms to malaria.

Subtertian malaria has very little tendency to relapse if it is properly treated, so-called relapses being nearly always due to reinfections. When malaria does relapse after the patient has left the endemic area the probability is, as the author points out, that there is a coincident benign or quartan infection.

All will admit that a great change has occurred in the therapeutics of malaria in the last 20 years. In the past, undoubtedly, too long and heavy courses of quinine were recommended, probably because relapse and reinfection were confused. The author has found that a course of 15 to 20 grains of quinine a day for 5 days and then 10 grains daily for a week, or of mepacrine 0·3 gm. daily for 5 to 7 days, followed by a similar course for a week, is quite sufficient. His own last attack in 1942 was treated with only 80 grains of quinine and there was no suggestion of a relapse.

In a series of cases where quinine and mepacrine were given to alternate patients little difference in results was found ; but it was noted that the latter was rather slower in its action and that parasites disappeared more slowly from the peripheral blood. Two cases of psychosis were noted after ordinary doses of mepacrine and it is thought that the larger doses now sometimes recommended are unwise ; no benefit was found from giving the two drugs together, and no treatment brought about disappearance of symptoms in less than 5 days in first attacks. Paludrine was not tried.

In chronic (usually recurrent) malaria, failing removal from the endemic area, each attack should be treated as it arises and a suppressive dose of mepacrine given daily.

Cerebral malaria has been found to be rare in European adults having efficient treatment, although it has been seen. It occurred most commonly in Group 2 cases, who have become careless. Blackwater fever usually occurred in Group 2 cases ; it was never seen in a first attack and followed as a rule irregular taking of quinine and also mepacrine. In contrast to cerebral malaria, it not uncommonly supervened in patients in hospital under treatment.

For cerebral malaria, it is thought that 5 grain doses of quinine given intravenously and repeated is the best treatment, although mepacrine has been used. In blackwater no specific was found, and sodium luminal in large doses intramuscularly did not reduce the mortality.

Malaria is a much more dangerous illness in children, especially infants, and here it does tend to be more " protean " in character. Withholding treatment while awaiting the result of blood examination is not recommended and it is important to give quinine or mepacrine, preferably by injection, at once in any suspicious case. Cerebral symptoms may develop very quickly, but the treatment of this complication is more satisfactory than in adults. In infants, the onset may be very insidious. [In the reviewer's experience this is especially true in breast-fed infants.]

The author considers the term " malignant " malaria is a bad one and unjustified. An occasional attack of subtertian malaria, if properly treated, makes little difference to the patient's general health. [The term malignant is probably a relic of bygone days, when mosquito control was almost nil, the condition often not recognized or badly treated, and repeated reinfections frequent. In these circumstances, it was a very fatal disease and blackwater was common ; for instance in the Gold Coast, where *circa* 1830 some 30 per cent. of new arrivals died in their first year, mostly from malaria and blackwater.]

Although no one is probably absolutely immune to this infection, some appear to have a higher resistance than others, although here the degree of personal anti-mosquito prophylaxis must be taken into account. Those leading the quiet life usually suffer less than those who are constantly out at night.

Those living under Group 1 conditions are not advised to take any drug prophylaxis, those under Group 2 to take a daily suppressive dose of mepacrine. Paludrine has not been tried by the author.

[This is such an excellent paper and so full of practical experience that the reviewer hesitates to make any criticisms. It is, however, suggested that :—

1. The author tends to underestimate the protean manifestations of malaria.
2. In many cases parasites are extremely hard to find within the first 2 to 3 days of illness.
3. Cerebral malaria does occur with a negative blood slide, even in adults.
4. Malaria tends to simulate the symptoms but not the physical signs of other diseases, *e.g.*, pain in the right iliac fossa, vomiting, possibly tenderness, but no rigidity and no diminution of peristaltic sounds.]

C. F. Shelton

HERNBERG, C. A. **Myocardial Affection in Malaria Tertiana.** *Acta Med. Scandinavica.* 1947, Nov. 5, v. 129, No. 2, 132–41, 6 figs.

In 1944, the author saw 9 cases of myocarditis among 596 people suffering from "malaria tertiana" [presumably benign tertian]. In three of these, electrocardiographic changes were uncertain; in the other six, which are described in detail, such changes did occur in some degree and included a reversible lowering of the S-T lead and a negativity of the T-wave: at times, the P-wave was changed.

The patients were all men between 20 and 40 years: three were farmers and one each was a stone-worker, a chauffeur and a sausage maker [and were thus all manual workers, for the most part in moderately heavy occupations]. Malaria parasites [presumably *P. vivax*] were found in the blood of each patient; on admission in 3 cases, and, in the others, on the 24th day, the 4th week and not "till a relapse occurred".

The nature of the myocardial lesion was manifested by the presence of praecordial oppression, tachycardia, changes in the heart sounds and an increased sedimentation rate. In only one case did permanent cardiac damage and insufficiency ensue.

The myocardial condition was seen, on an average, 43·5 days after the first attack of fever, and usually about a fortnight after the end of antimalarial treatment. The pathology of the condition is discussed and it is suggested that it may have been caused by blocking of the capillaries by malarial elements. No other cause was found: the patients were previously healthy soldiers on active service.

On the basis of the return to normal of the sedimentation rate, the disappearance of symptoms and stabilization of the Ecg., the active process in the heart appeared to occur over a period of 3–10 weeks.

H. J. O'D. Burke-Gaffney

CHEN, J. H. & WU, Y. K. **Transfusion Malaria and its Prevention by Quinine Therapy.** *Chinese Med. J.* Shanghai. 1946, Nov.–Dec., v. 64, Nos. 11/12, 309–14.

This report is based on 233 blood transfusions performed in the Chungking General Hospital. The blood was given to the patients immediately after withdrawal from the donors. It was difficult to get a reliable past history of malaria from these donors. One hundred and thirteen patients were given transfusions without quinine prophylaxis. Twenty-one developed malaria, 18 *P. vivax*, 3 *P. falciparum*. Five of the 21 patients had a history of past malaria; moreover the hospital is in an endemic malaria area.

The second group of 120 patients were given quinine by mouth as soon as possible after the transfusions, 0·3 gm. four times daily for from 5 to 7 days. None of these patients developed malaria in hospital.

The authors recommend the routine use of quinine after blood transfusions in an endemic area such as Chungking. *Norman White*

ROGERS, K. B. **Quartan Malaria transmitted by Blood-Transfusion. Report of a Case.** *Lancet.* 1947, Nov. 8, 688–9, 1 chart. [16 refs.]

It is recognized that malaria may be transmitted by blood transfusion and it has been suggested that persons who had lived in tropical or sub-tropical areas should not be used as donors if others can be found [this *Bulletin*, 1940, v. 37, 362, 456]. This question has become more obtrusive now that many ex-service persons are potential donors, and the author records a case which emphasizes the risk of using donors who have visited malarious areas, without having had clinical manifestations of the disease.

A young primipara, who had never travelled outside the county of Durham, received an antepartum transfusion of blood on March 8th 1946 : this consisted of 2 pints of homologous (A) blood which had been stored for 3 days. She was discharged without incident, and was delivered of a healthy full-term child on March 14th, at the same hospital. Except for one day of pyrexia, her puerperium was normal and she went home on March 24th.

Seven or eight weeks after the transfusion, she felt run down, sweated freely at night and eventually entered the county post-natal convalescent home on June 15th, with a " cold ". On 16th she had a slight rigor, which was repeated on 19th, 22nd and 25th : between the rigors, she felt well. On 25th, typical quartan malaria parasites were found in her blood : by this time, the patient was pale and had an easily palpable spleen and liver.

Blood examination, which was very full and is recorded in detail, revealed, *inter alia*, 3,600,000 red cells per cmm., 10·5 gm. Hb per 100 cc., and a blood sedimentation rate of 53 mm. in 1 hour (Wintrobe).

Agglutination tests and blood culture were negative. The patient was treated with quinine and mepacrine to which she responded rapidly : up to the age of 5 months, the child has shown no evidence of malaria.

There were two blood donors concerned. One had been on a cruise and had landed at Algiers for a few hours ; no parasites were found in her blood. The second donor was a ship's engineer who had been to Aden, Abadan and Basra for five months in 1939. He had never had malaria (but several members of the crew had " 3-day malaria " on the homeward voyage). On his return to Britain in the summer of 1939, he had bouts of feeling cold for short periods, and would go to bed for an hour during the day. He had not been out of England since and had no illness except " flu " during a local epidemic.

Examination of concentrated centrifuged blood from the second donor, by the author's technique [this *Bulletin*, 1946, v. 43, 392] revealed the presence of a definite male quartan gametocyte.

On July 4th, blood from both donors was injected into two patients with G.P.I., who belonged to blood-group A : no evidence of malaria has yet appeared in the patient who received blood from the first donor : the patient given the blood of the second donor developed malaria on August 5th. It is noted that although this donor was an active malaria carrier, his blood-sedimentation rate was not raised.

The author discusses the incidence of malaria transmitted by blood transfusion and surveys the relevant literature. He notes that the malaria transmitted by donors who have been absent from malarious areas for many years are nearly all quartan infections, though he mentions two benign tertian cases in the literature in which the donors had carried parasites for 3 and 10 years. He points out, with SHUTE [this *Bulletin*, 1944, v. 41, 1002), that quartan malaria is often no less common than the other varieties, and that it may be latent in persons from the tropics who act as donors. LOZNER and NEWHOUSER [*ibid.*, 91] have, however, shown that, when plasma is used, the risk of transmission of malaria is negligible : the author therefore suggests that persons who have been resident in malarious areas should not be bled for the production of whole blood for the purposes of transfusion. *H. J. O'D. Burke-Gaffney*

WINCKEL, C. W. F. **Quinine Injections in Malaria.** *J. Trop. Med. & Hyg.* 1947, Oct., v. 50, No. 10, 201–3.

The author considers that quinine will still hold its place against the newer synthetic antimalarial remedies for a considerable time.

Parenteral administration of quinine is held to be justified only : (1) When for some reason its oral use is impossible ; (2) to make sure that the drug is

actually being absorbed ; (3) in very severe cases (*e.g.* cerebral malaria) when the quickest possible action is necessary.

In (1) and (2), intramuscular, and in (3) intravenous, injections should be given.

Until recently, quinine dihydrochloride was the compound of choice, but as the author points out, the acidity (*p*H–3·5) of the solution tended to cause pain and necrosis of tissue, the latter predisposing to infection and abscess formation even after the greatest aseptic precautions.

The author recommends the less soluble hydrochloride salt according to the following prescriptions (for intramuscular use) :—

Quinine hydrochlor	8 grains (0·5 gm.)
Urethane	4 grains (0·25 gm.)
Aq. dest. ad	1 ml.
or Quinine hydrochlor	4 grains (0·25 gm.)
Antipyrin	2 grains (0·125 gm.)
Aq. dest ad	1 ml.

These solutions are nearly neutral and pain and necrosis are reduced to a minimum. The *p*H. of these solutions may be raised to that of the tissues (*p*H. 7·2) by adding a small amount of quinine base, this being the method used in the preparation of the German compound " Solvochin ".

The following prescription gives a solution very nearly approaching the alkalinity of the body tissues.

Quinine hydrochlor	45 grains (3 gm.)
Antipyrin	30 grains (2 gm.)
Sol. hydratis sodii norm. ...	0·75 ml.
Double-distilled water to ...	10·0 ml.

This is for intramuscular injection only. It may be diluted up to three times its original volume without causing precipitation of quinine ; it is not suitable for intravenous use. [No indication is given of the single dosage of this prescription which should be used.]

For intravenous use, the first two prescriptions should be diluted ten times and not more than 8 grains given at one time. Injections must be given slowly, one-tenth of the dose every minute.

[The use of quinine hydrochloride might with advantage be tried out more extensively, especially for intramuscular injection. The advantages are that the injections are painless, necrosis of tissues is insignificant and therefore danger of sepsis is greatly reduced.] *C. F. Shelton*

i. WINCKEL, C. W. F. **The Malaria Patient and Quinine.** *J. Trop. Med. & Hyg.* 1947, Nov., v. 50, No. 11, 219–20.

ii. J. TROP. MED. & HYG. 1947, Nov., v. 50, No. 11, 211–12. **The Route and Dosage in Antimalarial Therapy.**

i. The author doubts whether mepacrine, paludrine and chloroquine can yet be issued wholesale with safety to the populations of tropical malarious countries in the same way in which quinine has been sold and distributed by various governments.

It is remarked that British and American authorities have tended to recommend larger daily doses of quinine than continental ones ; the former generally advocate a daily dose of 30 grains or so. Thus MAEGRAITH (*Practitioner*, 1946, v. 157, 81) recommends 30 grains a day for two days, followed by 20 grains daily for the next five ; relapsed cases are treated with 30 grains combined with 30 mgm. pamaquin, daily for ten days ; the quinine is given either as a

solution of bisulphate or as tablets of the hydrochloride or bihydrochloride. The author notes that the bisulphate contains 59 per cent. of quinine base, the hydrochloride and bihydrochloride 82 per cent.

P. falciparum infections may require more quinine than those due to *P. vivax*, first attacks need larger doses than relapses, and a large discrepancy may exist on account of varying strains of plasmodia.

In the Netherlands East Indies, including parts of New Guinea, a daily dose of 22 grains of bisulphate or hydrochloride was found sufficient even for bad cases of *P. falciparum* infection, and in treating *P. vivax* a dosage of 15 grains was seldom exceeded. In 1932, in Java, Lichtenstein found that 9 grains daily of hydrochloride acted as well as 18 grains.

In Holland, the following treatment of *P. vivax* infections has been found successful ; 12 to 14 grains of quinine sulphate plus 45 to 54 mgm. pamaquin naphthoate (equal to about 30 mgm. pamaquin) are taken daily in 5 or 6 equal doses for 10 to 14 days. The author's point is that a small amount of quinine appears to be effective, and there appears to be no reason why moderate doses of this drug should not work as efficiently in other parts of the world as in Holland and the East Indies.

[The reviewer believes it to be now generally held that excessive and too prolonged dosage with quinine is unnecessary and may be harmful—*vide* experiences in Macedonia in 1917–18, when enormous doses of the drug were often given to malaria patients.]

ii. Two opposing views are put briefly in an editorial in the same *Journal*.

(1) The surest way of obtaining the full action of quinine is by intramuscular injection, and this should be the routine in treatment of malaria.

(2) Intramuscular injection is unnecessary and dangerous and little short of malpraxis.

The view expressed in the editorial is that the parenteral route is seldom necessary ; and when it is, intravenous quinine is preferable to intramuscular, but if the former is contraindicated the latter route may be used.

As pointed out by WINCKEL [above] the neutral hydrochloride salt is preferable to the highly acid and irritating bihydrochloride. The low solubility of the former may be overcome by addition of urethane and the resulting solution is nearly painless and non-irritating on intramuscular injection.

The danger of intravenous atebrin (mepacrine) is thought to have been exaggerated, but intramuscular injection seems to be just as effective, and the same applies to the newer synthetic drugs. As pointed out above there is a marked difference in the quinine base content of the various salts of quinine. During the recent war, there has been a tendency to re-introduce the prescribing of larger doses of quinine, one possible reason being that the amount prescribed was not actually being taken.

Investigations with the synthetic antimalarial drugs led to the practice of " loading " the first few doses so as to reach the necessary blood concentration in the shortest possible time, but with quinine this is not necessary. The writer of the editorial under review is uncertain whether the minimal doses of quinine recommended by Winckel will be generally adopted.

[The evil reputation of intramuscular quinine in the past has probably arisen from the experience of those working in parts of the world where *Cl. tetani* and other spore-bearing organisms are excessively common. Autoclaved sealed ampoules of quinine as supplied by any reliable firm of wholesale chemists are practically always sterile ; but difficulty may arise in the sterilization of needles and syringes, and the most careful precautions should be taken in this connexion.] *C. F. Shelton*

GHOSH, B. N. & GHOSH, T. K. **Chemotherapy of Malaria with special reference to Paludrine.** *J. Indian Med. Ass.* 1947, May, v. 16, No. 8, 267–9.

The authors discuss briefly the morbidity of malaria, the common anti-malarial drugs and the introduction of Paludrine: they then give a brief [but not very clearly stated] description of the biology of malaria parasites and the conceptions of the exo-erythrocytic phases, together with their therapeutic implications.

The authors then report the use of paludrine by them in 50 cases of malaria, which could be followed up and supervised for a prolonged period. Their results are summarized as follows:—

Average daily dose	Total dose for the course	Day of disappearance of fever	Day of disappearance of parasite	Relapse checked with periodic use
100 mg. to 200 mg.	300 mg. to 700 mg.	2nd day (90 per cent.)	2nd/3rd day (80 per cent.)	90 per cent.

It is stated that the drug is generally given in tablets of 100 mgm. twice a day for two or three days until the fever subsides: except for slight nausea, "which is not felt when taken with a glass of water", no toxic symptoms were observed; no untoward effect was observed when the drug was used in the case of two pregnant women.

"In malignant malaria it will cause definite cure. But relapses may occur in benign tertian after a few days when it may be used twice a week for 3–6 months to stop it."

The authors discuss the estimated quinine needs of India and compare them with the economic advantages of paludrine.

They finally draw a number of conclusions regarding paludrine which accord, in general, with those of many other observers: but these conclusions do not all follow from the somewhat scanty experimental records provided in the paper. [The authors do not give details of their cases or the types of malaria of which they consisted: conclusions regarding prophylaxis and suppression are drawn, without provision of experimental evidence on which to support them. See also this *Bulletin*, 1948, v. 45, 34–6.] *H. J. O'D. Burke-Gaffney*

COOPER, W. C. & COATNEY, G. R. **Studies in Human Malaria. III. The Therapeutic Effect of a Phenanthrene Amino Alcohol, NIH-204 (SN-1796), in Vivax, Falciparum, and Quartan Malaria.** *Amer. J. Hyg.* 1947, July, v. 46, No. 1, 119–31, 2 figs.

The chemical formula of NIH-204 is 9-(2-diamylamino-1-hydroxyethyl)-1, 2, 3, 4-tetrahydrophenanthrene hydrochloride. This report summarizes the treatment of 66 malaria attacks in 47 patients undergoing therapeutic malaria in a mental hospital. Fifty-one attacks were due to *P. vivax*. In these infections, 0·5 gm. of NIH-204 or more a day, for 6 days, relieved the clinical attack and reduced parasitaemia to subpatent levels in all but one instance. Relapses occurred after treatment of all sporozoite-induced early attacks, regardless of dosage. Prompt relapses (4 to 27 days after treatment) appeared after all early attacks treated with 0·25 gm. daily and in the majority treated with 0·5 gm. daily, but after only 3 of 16 attacks treated with 0·9 gm. daily; relapses in the 13 other cases were delayed, 153 to 273 days.

Thirteen attacks due to *P. falciparum* were treated with NIH-204. The doses were 0·96 gm. daily in 10 cases, 1·5 gm. daily in 3 cases. In all but one

instance there was parasite and clinical response. The clearance of parasites and subsidence of fever were generally slow in primary attacks. Early relapses occurred after 5 of the 6 primary attacks and after 2 of 4 first relapses.

Two blood-induced *P. malariae* infections were treated with NIH-204; parasites disappeared and fever subsided in both. There was no relapse during 4 years of observation.

Symptoms of intolerance noted were lowering of the threshold of pilomotor stimulation, in most cases; marked but asymptomatic bradycardia in 42 cases; difficulty in passing urine in 8 cases, and microscopic haematuria in 17.

At the doses used, which were near the limit of tolerance, NIH-20 is certainly no better than quinine and definitely inferior to mepacrine in the treatment of *P. vivax* malaria. It is inferior to both drugs in the treatment of *P. falciparum* infections. *Norman White*

DECOURT, P. & SCHNEIDER, J. Traitement curatif du paludisme par divers sels du 3-méthyl-4 (diéthylaminopentyl) amino-7-chloroquinoléine (nivaquine). [**Curative Treatment of Malaria with various Salts of 3-Methyl-4 (Diethylaminopentyl) Amino-7-Chloroquinoline (Nivaquine).**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 1/2, 14–17.

Three salts of nivaquine, the composition of which is indicated in the title to this paper, have been tested in the treatment of malaria in Tunisia; a methylene bis-oxynaphthoate, Nivaquine M; a resorcin-carbonate, Nivaquine R; a dichlorhydrate, Nivaquine C. Nivaquine was formerly known as Sontoquine.

More than 150 patients have been treated with Nivaquine M. The average dose was 0·6 gm. a day for 5 days. Fever was controlled in 36 hours and schizonts disappeared from the peripheral blood in 48 hours.

Nivaquine R was used in the treatment of only 17 patients. The results were very much less favourable than those obtained with Nivaquine M.

Nivaquine C was much more active in the treatment of malaria than either of the two other preparations. More than 200 patients have been treated with it. The daily dose in cases of average severity was 0·3 gm. A daily dose of as little as 0·08 gm. is sufficient to arrest the attack; 0·1 gm. of quinacrine is necessary to secure the same result. Patients treated for 5 to 7 days are always apyretic at the end of 36 hours; no relapses were noted in the several weeks during which the patients were under observation. All doses in this paper are doses of base. *Norman White*

KING, H. & TONKIN, Isabel M. **Antiplasmodial Action and Chemical Constitution. Part VIII. Guanidines and Diguanides.** *J. Chem. Soc.* 1946, Nov., 1063–9.

BARBER, H. J. & WRAGG, W. R. **Contributions to the Chemistry of Synthetic Antimalarials. Part IV. Hydrazine Hydrolysis and Radical Exchange Reactions of N-Substituted Phthalimides in relation to the Constitution of the Antimalarial R.63.** *J. Chem. Soc.* 1947, Oct., 1331–7.

BASFORD, F. R., CURD, F. H. S., HOGGARTH, E. & ROSE, F. L. **Synthetic Antimalarials. Part XXI, 4-Arylamino-6-Aminoalkylaminopyrimidines. Further Variations.** *J. Chem. Soc.* 1947, Oct., 1354–64.

DE MEILLON, B. & THORP, J. M. **The Inhibition of Growth of Larvae of *Aedes aegypti* by certain Anti-Malarial Drugs.** *South African J. Med. Sci.* 1947, Jan., v. 12, No. 1, 33–8.

In this paper are recorded the results of experiments which demonstrate the inhibition of the growth of the larvae of *Aëdes aegypti* by quinine and atebrin [mepacrine] and the reversal of this inhibition by dietary means. This work has followed on that of MADINAVEITIA [this *Bulletin*, 1946, v. 43, 1011], who found that antimalarial drugs inhibit the growth of *Lactobacillus casei*, and HELLERMAN *et al.* [*ibid.*, 1947, v. 44, 400], who showed that adenylic acid could reverse the inhibitory effect of quinacrine on the growth of *Plasmodium lophurae*. The object of this paper was to examine the relation of these effects of antimalarials to living systems other than micro-organisms.

In an adequate medium containing minimal quantities of brewer's yeast and a vitamin mixture, reversal of inhibition was attained by increasing the yeast fivefold or by the addition of the water-soluble fraction of yeast; definite reversal did not follow an increase in concentration of the vitamin content, namely thiamin chloride, riboflavin, pyrodoxin, pantothenic acid and nicotinic acid. *R. Ford Tredre*

GOLBERG, L. & DE MEILLON, B. **Further Observations on the Nutritional Requirements of the Larva of *Aedes aegypti* L.** *Nature.* 1947, Oct. 25, 582–3, 1 fig. [See also DE MEILLON & THORP, above. Detailed findings will be furnished later.]

PACKER, H. **Experimental Field-Type Suppression with SN 7618 (Chloroquine), SN 8137 and SN 12,837 (Paludrine).** *J. National Malaria Soc.* 1947, June, v. 6, No. 2, 147–54.

These observations were carried out on white neurosyphilitic patients, without a previous history of malaria, who had been admitted to hospital for malaria-therapy. The McCoy strain of *P. vivax* and the Costa strain of *P. falciparum* were used, and insectary-bred *A. quadrimaculatus* was the vector.

Twelve patients received weekly doses of SN 8137, from 0·125 to 0·5 gm., without a priming dose. They were given mosquito inoculations of *P. vivax* on three alternate days of the first week, the first weekly dose of drug being given the day before the first inoculation. The weekly dose of drug was continued during three consecutive weeks following the week of inoculations. The minimum effective weekly suppressive dose was found to be between 0·125 and 0·25 gm. No break-through occurred when the higher dose was given.

Equivalent doses of SN 7618 (chloroquine) were not so effective against *P. vivax*: break-throughs occurred with 0·25 gm. weekly. If, however, a priming dose of double the weekly maintenance dose was given a week before the week of inoculations the results obtained were similar to those obtained with SN 8137.

The minimum effective dose of paludrine against *P. vivax* was not determined, but observations on four patients showed that the amount of the drug required is no more than one-third of the effective doses of SN 8137 and SN 7618.

Against *P. falciparum*, paludrine was found to exercise suppressive action comparable with that of chloroquine in doses three times as large. *P. falciparum* infections require higher doses of either drug for effective suppression than do *P. vivax* infections.

Paludrine given on any day between the first and fifth days, inclusive, after *P. falciparum* mosquito inoculation gives protection. If given on the sixth or seventh days, infection breaks through. This confirms Fairley's observation

that paludrine is a true causal prophylactic in *P. falciparum* malaria ; and is more active against pre-erythrocytic forms than against the erythrocytic stages of the parasite. *Norman White*

i. COATNEY, G. R., COOPER, W. C., YOUNG, M. D. & MCLENDON, S. B. **Studies in Human Malaria. I. The Protective Action of Sulfadiazine and Sulfapyrazine against Sporozoite-induced Falciparum Malaria.** *Amer. J. Hyg.* 1947, July, v. 46, No. 1, 84–104. [17 refs.]

ii. ——, ——, ——, BURGESS, R. W. & SMARR, R. G. **II. The Suppressive Action of Sulfadiazine and Sulfapyrazine against Sporozoite-induced Vivax Malaria St. Elizabeth Strain).** *Ibid.* 105–18, 1 fig. [29 refs.]

iii. ——, ——, —— & ——. **IV. The Suppressive Action of a Phenanthrene Amino Alcohol, NIH-204 (SN-1796), against Sporozoite-induced Vivax Malaria (St. Elizabeth Strain).** *Ibid.* 132–40, 2 figs.

i. I.—These investigations were carried out in 1942–43. For the *P. falciparum* investigation, the subjects were selected from white and Negro male patients in two large mental hospitals. The McLendon strain of *P. falciparum* was used. This was isolated from a patient in South Carolina in 1940. Insectary-reared *A. quadrimaculatus* were used as vectors. Sulphadiazine and sulphapyrazine were given in 0·5 gm. tablets. In all but one test, administration of the drug was begun before exposure to infection. The tests involved 75 treated and 36 control subjects. Sulphadiazine in doses of 12 gm. a day continued for 46 hours after exposure, with blood concentrations over 20 mgm. per 100 ml., did not act as a causal prophylactic of *P. falciparum* malaria ; the prepatent and incubation periods were, however, doubled. Four grammes daily for 6 days after exposure, or 2 gm. daily for 5 days or 10 days, produced delay of patent infection. Four grammes daily for 11 days after exposure prevented infection in 4 of 5 patients. Four grammes daily for 42 days after exposure protected all of 10 patients : 2 gm. daily for the same period 9 out of 10 : 1 gm. daily for the same period protected 8 out of 9 : 0·5 gm. daily for the same period prevented patent parasitaemia and clinical attacks in 3 of 5 subjects, but borderline clinical symptoms occurred. The minimum blood concentration of sulphadiazine associated with suppression was approximately 1·1 mgm. per 100 ml.

One-half gramme of sulphapyrazine daily for 42 days after exposure gave results similar to those given by the same dose of sulphadiazine.

As a suppressive of *P. falciparum* malaria sulphadiazine possesses no advantages over atebrin [mepacrine].

ii. II.—Similar observations were carried out on white male patients infected with the St. Elizabeth strain of *P. vivax*. Sulphadiazine 3 gm. daily, for 2 days before and 42 days after infective mosquito bites, did not prevent infection in any of 10 patients. Mean minimum blood concentrations of over 5·0 mgm. per 100 ml. were suppressive ; in 4 patients, malaria appeared 9 to 11 months after infection. With smaller doses the majority of patients developed clinical attacks while receiving treatment. Sulphapyrazine, in daily doses of 1·0 and 0·5 gm., was similarly ineffective. With these drugs, *P. vivax* malaria is far more difficult to suppress or prevent than is *P. falciparum* malaria. Both drugs are poor suppressants of the strain of *P. vivax* used, compared with either quinine or mepacrine.

iii. IV. In this study 30 white patients were observed. The suppressive action of NIH-204 (SN-1796)—a phenanthrene amino-alcohol—was compared with that of mepacrine against *P. vivax* infection. There were ten patients in each of the two groups and ten controls who received no protective medication. NIH-204 was given in capsules containing 0·15 gm. of the hydrochloride

(91·2 per cent. base). Quinacrine [mepacrine] dihydrochloride was given in standard 0·1 gm. tablets. Each man was bitten by from 3 to 7 infected mosquitoes on each of 3 days spaced evenly over a week. NIH-204, 0·3 gm. daily, for 2 days before, 7 days during, and 28 days after the week of infection, effectively suppressed *P. vivax* malaria, as did quinacrine hydrochloride 0·1 gm. daily commencing 8 days before the week of infection. All of the subjects developed delayed primary attacks 6 to 10 months after exposure to infection. NIH-204 is not recommended for the field suppression of malaria because of annoying side-actions that accompany its use, and because better suppressants are available. The side-actions were lowering of the threshold of pilomotor stimulation; slowing of the pulse; difficulty in urination, and microscopic haematuria. *Norman White*

MISSIROLI, A. Riduzione o eradicazione degli anofeli? [**Reduction or Eradication of Anophelines?**] *Riv. di Parassit.* Rome. 1947, June–Sept., v. 8, Nos. 2/3, 141–69, 9 figs. English summary (7 lines).

In the autumn of 1943 there were large inundations of parts of the Tyrrhenian seaboard of Italy owing to the war. Breeding of mosquitoes increased and, in addition, the percentages of *Anopheles maculipennis labranchiae* rose to nearly 100 per cent. in some areas. The result was a great increase in the incidence of malaria. A new method of attack on this old problem was attempted with the aid of funds and equipment from UNRRA and other sources. Instead of anti-larval treatments and other measures, reliance was placed on anti-adult spray-painting of houses and animal sheds with DDT.

The method has proved so successful that a five-year plan has been started to eradicate malaria from Italy. The country falls into four distinct regions differing in their particular malaria problems. (I) The northern plain of Lombardy has only local patches of malaria, due to *Anopheles maculipennis atroparvus*. (II) The coastal region of the northern end of the Adriatic has malaria spread by *A. sacharovi*. (III) The central part of Italy suffers from malaria spread by *A. m. labranchiae* which occurs along the coast of Tuscany and Lazia at places below 300 m. above sea level. (IV) The southern part of Italy as well as Sicily and Sardinia constitute the most difficult problem, for malaria spread by *A. m. labranchiae* is common everywhere in regions below 1,000 m. above sea level.

The aim of the plan is to treat all houses in the malarious patches of zones I, II and III in the first year; in the second year, to deal with the western, and in the third year the eastern halves of zone IV.

Results of work completed so far are given in graphs which show the monthly statistics for certain areas in 1945 (before DDT spraying) and in 1946 (afterwards). The graphs show striking declines in numbers of mosquitoes at catching stations, reported cases of malaria, positive blood films, deaths from malaria and also from all causes. The decline from all causes is due to the absence of a peak during the summer months in the year of DDT spraying. This appears to be due not so much to the effect on malaria as to a reduction of enteric diseases consequent on the widespread destruction of houseflies achieved by the DDT. Figures are also given of parasite rates and spleen indices for March 1946 and March 1947.

The author briefly discusses the possibility of eradication of mosquitoes and remarks that further judgment can be made at the end of an eradication campaign now in progress in Sardinia. He concludes that it would take fifteen years at least to do such a thing in Italy itself and would be exceedingly costly. On the other hand, the use of DDT spray-painting was easier and cheaper, and affected flies and other parasites as well as mosquitoes. An indication of a race

of flies with unusual resistance to DDT complicated the picture, but it appears that they may be attacked with other, similar, insecticides. *J. R. Busvine*

PUTNAM, P. & HACKETT, L. W. **An Appraisal of Malaria Reduction in Albania, 1929–1938.** *J. National Malaria Soc.* 1947, June, v. 6, No. 2, 131–46, 7 figs.

Malarial surveys and antilarval measures were started in Albania in 1929 by the Health Department of that country, under the auspices of the International Health Division of the Rockefeller Foundation. Antilarval schemes were carried out in Tirana, the capital, Durazzo, its port, two inland towns, Elbasan and Berat, and the coastal town Valona. Kavaja, a coastal town just south of Durazzo, was used as a control area. Annual surveys of school children, from 5 to 12 years of age, were made in February or March in all these towns.

Anopheles sacharovi is the important vector of malaria in the coastal plains, where it breeds in the salty lagoons. *A. maculipennis maculipennis* and *A. m. subalpinus* were found wherever collections were made. *A. m. messeae* is a highland species. *A. superpictus* was found breeding extensively in the gravel beds of torrents during the dry summer. *A. maculipennis* (*maculipennis* and *subalpinus*) could be captured throughout the year but the high peak of prevalence occurred in June and July. *A. sacharovi* was prevalent in May, June and July, the shortness of the season being due to the increased salinity of the breeding grounds in the dry season. The seasonal prevalence of *A. superpictus* was irregular. The prevalence curve showed two peaks each year, but specimens could be captured in any month.

At Tirana, where *A. superpictus* is the chief vector, swamps were drained and all the river water was diverted above the town into a well-regulated irrigation system throughout the breeding season. At Durazzo the salinity of the lagoon was increased by admitting sea water at high tide. At Elbasan and Berat, paris green was used extensively. At Valona filling and draining of swamps and lagoons were commenced but progress was slow.

The reduction in malaria is appraised by statistical methods. A reduction occurred in each of the protected areas, greatest in Tirana and Durazzo where permanent measures were possible. In Tirana the density of *A. superpictus* dropped sharply from 1932 to 1938 while that of *A. maculipennis* remained constant. In Elbasan and Berat, the density of both species decreased. In Valona there was no decrease either in *A. sacharovi* captures or in parasite rates.

Norman White

i. AZIZ ,M. **Report on the Anopheles (Malaria) Eradication Scheme Karpas-Cyprus 1946.** 67 pp., numerous graphs & charts & 35 figs. 1947. Nicosia: Cyprus Govt. Printing Office.

ii. ——. **A Brief Account of the Anopheles (Malaria) Eradication in Karpas-Cyprus, 1946.** *J. Roy. San. Inst.* 1947, Sept., v. 67, No. 5, 498–509, 3 figs.

i. The first stage of an attempt to eradicate anopheline mosquitoes and malaria from the island of Cyprus has been completed. The story is told in full in the first paper and summarized in the second.

The area chosen for the first season's work, 1st April to 16th November 1946, was the Karpas, the narrow tongue of land to the north-east of the island, the topography of which is described. It consists of about 450–500 square miles, but an additional inland protective area of some 250 square miles was also included and placed under control as a protection against anopheles infiltration. In the rest of the island, the usual routine control, limited to 1½ miles around towns and villages, was continued. The population of both areas is 34,000,

living in 65 villages. The anophelines are *A. superpictus*, *claviger*, *sacharovi*, *algeriensis*, *marteri* and *hyrcanus*; *A. multicolor* occurs in other parts of the island. The three first named are known to be vectors of malaria, *A. superpictus* being responsible for 95 per cent. of the rural malaria. In the island there is an average of 10,500 cases per annum with 18,000 in some years.

The recruitment of staff, organization of the eradication scheme and the duties of each member are described. When complete, the staff consisted of an executive officer and his assistants, a district officer, 2 headquarters inspectors, 4 section officers, 1 malaria technician, 2 field inspectors, 8 zone officers, 1 storekeeper, 3 clerks and between 75 and 80 labourers. The relationship between the workers had to be understood by all; the checking and counter-checking of each other's work formed an essential part of the scheme and had to be undertaken without bad feeling or suspicion. Those accustomed to ordinary control work had to become "eradication-minded" and had to be continually impressed with the necessity for negative reports. The many difficulties encountered, and how they were overcome, are described in some detail. For example, it was not possible to continue with routine treatment of vehicles travelling through the area until the public health legislation had been amended, and by that time it was too late to be effective. Some of the staff deserted for less hazardous occupations, but this was counteracted to some extent by the issue of free clothing, boots, soap and so on.

The area was divided into 51 blocks of 10 to 30 square miles each, though the sizes had to be adjusted in the light of experience as the work progressed; in each block were 12 plots and one labourer was expected to do one plot per day. Blocks were grouped into 10 zones and the whole peninsula into 4 sections. Most attention was given to breeding places; these were dotted over many places; some of them were very difficult to reach. At first, DDT residual spraying was not done, but "ordinary insecticide" was used in houses, stables, etc. as it was not possible to treat buildings properly because there were many rooms to which the operators were not admitted; later, a "light DDT spray" was used in adult resting places as the weather got colder.

The materials used were: against larvae, 8,416 gallons of 4 to 5 per cent. DDT in gas oil (fuel oil); against adults, 160 gallons of 3 per cent. DDT in gas oil; "ordinary insecticide" [? pyrethrum] 168 gallons; 193 larvicide sprayers (lengthened flit guns) and 84 standard flit guns, all made locally. The cost to 31st October 1946 was £12,000. Monthly progress was recorded in tables and on maps, until finally it was possible to show that no anopheline mosquitoes had been reported between 6th October and 16th November 1946.

The text occupies 14 foolscap pages but there are 40 pages of tables, charts, maps, and samples of the forms used as well as 35 photographs.

ii. The second paper is a shortened version of the first. It was read before the Tropical Hygiene Section of the Health Congress of the Royal Sanitary Institute, in June 1947.

A careful search of the 1946 eradication area has, up to 10th February 1947, revealed no adults and no larvae of *A. superpictus*; a few larvae of *A. claviger* and *A. marteri* have been found in isolated waters.

In this paper, the total cost of the scheme for 1946 is put at £18,000, which represents ten shillings per head of the population or £36 per square mile.

In the discussion following the paper, it was pointed out that the work in Cyprus emphasized once again the fact that every malaria problem is a local one. This was illustrated by one point, that in the *superpictus* eradication work the flit type of sprayer suited the conditions in Cyprus and was the most economical; isolated patches of water could not be economically dealt with by the drop method as used in the Sudan. The author was unable to give figures for the amount of DDT used per acre, but the amount of larvicide used by one man per

day averaged about one gallon. Wells were treated with the same larvicide as surface water, and it was also used to spray the sides of the wells to kill resting adults.

The campaign for 1947 is planned to take in half the island, and in preparation, a winter scheme is in progress consisting of an attack on adult harbourages with DDT in gas oil. *H. S. Leeson*

PURI, I. M.; RAJINDAR PAL; KRISHNASWAMI, A. K.; BHATIA, M. L. **Studies on some Insecticides against Anopheline Adults and Larvae. I. Preliminary Experiments at Delhi with DDT** [PURI & RAJINDAR PAL]. *Indian J. Malariology.* 1947, Mar., v. 1, No. 1, 133–58, 7 graphs. [16 refs.]. **II. DDT as Residual and Space Spray and as Larvicide** [PURI & KRISHNASWAMI]. *Ibid.* 159–81, 26 graphs. **III. Experiment with DDT as a Residual Spray in some Villages in Baluchistan** [PURI & BHATIA]. *Ibid.* 183–91, 3 graphs. **IV. Experiments with DDT and 666 as Residual Spray in some Villages around Delhi in 1946** [PURI & KRISHNASWAMI]. *Ibid.* 193–209, 7 graphs.

Staff of the Malaria Institute of India have conducted experiments to assess the potentialities of DDT as a mosquitocide and larvicide and to study methods of application under Indian conditions. Their results are largely confirmatory of the work of workers in other countries, but in publishing them they have performed a valuable service for field workers in India.

Part I. Preliminary Experiments at Delhi with DDT

The materials used were mainly 5 per cent. DDT solution in kerosene, malariol or used engine oil, and a DDT-turpentine emulsion; the method of preparation is fully described. The results were as follows:—

Larvicide: (*a*) DDT in oil was "very effective" in doses of 4 to 6 cc. per 10 sq. yards.

(*b*) DDT-turpentine emulsion is "more effective" than (*a*): thus, 2 to 4 cc. of 5 per cent. emulsion (100 to 200 mgm. of DDT) per 10 sq. yds. gave 100 per cent. control for 5 to 8 days and partial control for 12 days.

(*c*) Aerial spraying is "wasteful and very erratic".

Residual Insecticide: Both oil and emulsion produced, in mud huts, a 100 per cent. reduction in adult mosquitoes during the first four days, with a partial residual effect persisting for four to five weeks; the dose was 150 mgm. to 200 mgm. per sq. foot.

Part II

1. *DDT as Larvicide. Nilgiris, South India*

Tabulated results show the effect of 5 per cent. DDT in a turpentine emulsion and in solution in kerosene, used engine oil and malariol, when applied to flowing streams, to still water in pits and to fallow or growing ricefields. In still water, 0·6 cc. of solution per 10 sq. yds., as compared to 3 to 4 cc. in stream or ricefield, was sufficient to produce 100 per cent. kill. A residual effect for 6 to 8 days was evident in ricefields with doses of 2 to 5 cc. of 5 per cent. solution per 10 sq. yards. Higher aquatic fauna appeared to be unaffected.

2. *DDT as an indoor residual spray. Bengal, Terai*

Graphs illustrate the effect on indoor anopheline populations of a single application of a 5 per cent. solution or emulsion at a dose of 1 quart per 1,000 sq. ft. of mud plaster surface. Results for solution or emulsion were similar at nearly 100 per cent. reduction for a number of days, the residual

toxicity lasting for two months ; increased dosage did not lengthen this period. *A. minimus* was more sensitive to the residual action than other anophelines.

3. *DDT as an outdoor residual spray. Bengal, Terai*

Bushes, fences, lanes and the outer surfaces of walls and roofs of huts in a 50-yard belt surrounding groups of dwellings were sprayed with the various 5 per cent. DDT solutions or emulsion. Results are depicted graphically and indicate that a dose of 1 to 3 gallons per acre caused an appreciable reduction in the indoor mosquito population for periods up to 13 days ; *A. minimus* in particular reappeared later than other mosquitoes. Rainfall vitiated the residual action.

4. *DDT as a space spray* (5 per cent. DDT-kerosene solution). *Bengal, Terai*

This solution used in the interior of dwellings twice a week for three months resulted in a marked reduction of the sporozoite rate among *A. minimus*. As a malaria control measure this is as effective as the use of pyrethrum spray.

Part III

Quetta (Baluchistan) was selected for further experiments with DDT as a residual indoor spray, because it differed from previous areas of Papers I and II in having a short malaria and mosquito season, and in having *A. superpictus* as the main vector mosquito. A dose of 50 mgm. per sq. ft. reduced the mosquito population to negligible numbers for 10 weeks.

A dose of 25 mgm. per sq. ft. though not producing a 100 per cent. reduction in numbers of mosquitoes, did appear to reduce the sporozoite rate among *A. superpictus* present.

Part IV

Experiments were conducted in the Delhi area to compare the efficiency of DDT and Gammexane as residual insecticides. The authors, although making observations on the results with DDT, were not prepared to express an opinion on Gammexane because " the experimental conditions under which this test was carried out " did not permit it. *R. Ford Tredre*

PURI, I. M. **The Practical Application of DDT for Malaria Control in Rural and Urban Areas in India.** *Indian J. Malariology.* 1947, Mar., v. 1, No. 1, 211–20.

This paper summarizes the previous four and has reference to costs which are of little assistance outside India. *R. Ford Tredre*

BRESCIA, F. & WILSON, I. B. **Treatment of Native Villages with the Aerosol Generator.** *J. Econom. Entom.* 1947, June, v. 40, No. 3, 313–16.

[The paper begins with the alarming phrase " Two villages were treated to determine whether an oil-DDT aerosol generated outside native huts can kill adults resting inside the huts during the course of treatment . . . " It seems, however, that mosquito adults are implied.]

The villages were thatched native villages in the Solomon Islands. No details of the generator are given, but it is stated that it produces an aerosol with particles of 10-microns diameter. A dosage of 5 lb. DDT per 1,000 feet of front was sufficient to destroy *Anopheles farauti* inside and outside the huts and to kill larvae ; but it only gave a protective period of five days in one village and one day in another. [The front is the distance covered by the generator carrier.] To obtain " an appreciable " protective period it is necessary to use 20 lb. of DDT per 1,000 feet of front (the front extending 2,000 ft. beyond the

village), if breeding occurs in pools over 1,000 feet from the village. Where breeding is restricted to pools less than 1,000 feet from the village, a dosage of 10 lb. DDT should suffice. *J. R. Busvine*

HINMAN, E. H. & CUTKOMP, L. K. **Block Residual Spraying of Premises with DDT for the Control of Malaria.** *Amer. J. Trop. Med.* 1947, July, v. 27, No. 4, 449–61, 1 map.

As a result of the experimental work by HESS and KEENER [this *Bulletin*, 1947, v. 44, 880] in the Tennessee Valley, the DDT residual spray technique has been applied to an area adjacent to the Wheeler Reservoir (Tennessee Valley Authority) in North Alabama (35°N. 87°W.), a neighbouring area being used for control purposes. The treated district contained 299 occupied premises in 38 sq. miles, compared with 238 in 33 sq. miles in the untreated control district. Approximately the same percentage of mosquito-proofed residences were present in the two districts.

The interiors of all types of structures (houses, barns, privies, animal habitations etc.) were treated with 5 per cent. emulsion of DDT (Stock solution 25 per cent. DDT, 73 per cent. Xylene, 2 per cent. Triton) by means of knapsack sprayers; rate of application approximated 200 mgm. of DDT per sq. foot; costs, excluding supervision, were at the rate of 0·91 dollar per 1,000 sq. feet.

The reduction in numbers of the vector anopheline, *A. quadrimaculatus*, is evident in the following table.

Average number of A. quadrimaculatus mosquitoes per premise

Area	Pre-Treatment Inspection	Post-Treatment Inspections								
	June	July			August			September		
		1	2	3	4	5	6	7	8	9
Sprayed ...	20·09	0·4	0·4	0·9	1·1	1·2	1·2	2·1	2·8	6·2
Control ...	23·3	32·9	32·1	35·6	43·8	31·1	13·1	15·1	29·4	14·2

The figures are based on the total numbers caught in all structures on a premise.

Catches of adult mosquitoes in certain unsprayed sections of barns and in well-placed traps, and larval density surveys in adjacent breeding waters, showed that high production of mosquitoes continued despite the premise spraying.

Examination of thick blood films of 90 per cent. of the inhabitants of both districts was completely negative, and no conclusion is possible on the effect of the spraying on malaria transmission.

As a result of this experiment and previous information on human blood-feeding of *A. quadrimaculatus*, the authors are of opinion that DDT residual spraying of all structures offers more protection against malaria transmission than mosquito-proofing. *R. Ford Tredre*

CUTKOMP, L. K. **Residual Sprays to control** *Anopheles quadrimaculatus*. *J. Econom. Entom.* 1947, June, v. 40, No. 3, 328–33, 3 figs.

The paper reports tests, in the laboratory and in unoccupied houses, of various insecticides applied at rates of 100–250 mgm. per sq. ft. The toxicity at different

times was judged by the exposure period necessary to cause knockdown of *A. quadrimaculatus*, the experience of the author being that mosquitoes thus affected never recovered (except, sometimes, with pyrethrins).

The results showed pyrethrins and then *gamma* benzene hexachloride to be most toxic according to this criterion, followed by DDT and "Chlordane" ($C_{10}H_6Cl_8$) and, finally, "Toxaphene" ($C_{10}H_{10}Cl_8$). The residual action of DDT was greatest, followed by those of benzene hexachloride and "Toxaphene", which declined somewhat after fifteen weeks but, under some conditions, were still effective at the end of a year. Pyrethrins and "Chlordane" were least persistent.

An experiment was performed to compare the irritant effects of the various insecticides, calculating the percentages of mosquitoes leaving treated houses in which they were liberated. The figures observed were :—

Houses treated with—

Pyrethrins	(200 mgm./sq. ft.)	80 per cent. left the houses
DDT	250 ,, ,,	57 ,, ,, ,, ,, ,,
Benzene hexachloride	100 ,, ,,	8·3 ,, ,, ,, ,, ,,
"Toxaphene" ...	160 ,, ,,	3·5 ,, ,, ,, ,, ,,

J. R. Busvine

DAVIDSON, G. **Field Trials with "Gammexane" as a means of Malaria Control by Adult Mosquito Destruction in Sierra Leone. I. The Effect of "Gammexane" on Mosquitoes.** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 178–209, 2 maps, 2 text figs. & 12 figs. on 3 pls.

The insecticidal properties of hexachlorocyclohexane (benzene hexachloride, $C_6H_6Cl_6$) were first noted in 1942 by Imperial Chemical Industries Ltd., and in 1943 the active insecticidal constituent, the gamma isomer, Gammexane, was isolated.

Various workers showed by laboratory experiment that Gammexane is lethal to mosquitoes in smaller concentrations than DDT, and is quicker in its action.

This paper describes experiments conducted in Sierra Leone to measure the true value of Gammexane for the destruction of adult *Anopheles gambiae*, *A. funestus* and *A. melas* by the residual insecticide method.

Three groups of villages were selected :

(*a*) A coastal group at the foot of the mountains on the open sea.

(*b*) An inland group in the Protectorate associated with mining.

(*c*) A single large village on the Freetown estuary.

Smoke Generators containing Gammexane : A trial of this method in four villages proved it to be inefficient, mainly because of the impossibility of sealing the type of house.

Residual Sprays containing Gammexane : Detailed description is given of products used, machines for, and technique of spraying. The walls of houses had a variety of surfaces, wood, mud, thatch, concrete, and corrugated iron.

A detailed analysis of the results in each sprayed village and of the variations of mosquito density in the unsprayed control villages is given. These results may be summarized as follows :—

1. Gammexane in the form of a residual spray is an efficient means of reducing the population of mosquitoes in houses.

2. 0·5 per cent. solution applied at rate of 10 mgm. per square foot (4 pints of solution or mixture to 1,000 sq. ft.) to every available internal wall surface of all houses will reduce the mosquito population in the houses to almost nil for a period of six months.

3. A lowering of mosquito density in unsprayed houses in adjacent areas was noted.

4. In admittedly small numbers of dissections, 247 from treated and 159 from untreated villages, the sporozoite rate was 2 per cent. in the former, compared to 4·4 per cent. in the latter.

R. Ford Tredre

DAVIDSON, G. **Field Trials with "Gammexane" as a means of Malaria Control by Adult Mosquito Destruction in Sierra Leone. II. The Effect of Treatments of Houses with "Gammexane" on the Malaria-Rate in the Inhabitants.** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 210–14.

By the fowl-cell technique of Christophers, Sinton and Covell, malaria parasite count distribution, in addition to parasite rate, was estimated from the blood of children in the 0–10 years age-group in selected groups of villages before, and five months after, spraying with Gammexane [see preceding abstract].

The results may be summarized as follows:—

Locality	No. Examined	Parasite Rate per cent.	Parasite-count distribution (No. per cmm.)			
			0–500 per cent.	500–1,000 per cent.	1,000–3,000 per cent.	Over 3,000 per cent.
Coastal Villages						
Before treatment ...	189	81·5	65	9	11	15
After treatment ...	111	80·2	50	9	20	21
Untreated	68	88·2	40	34	13	13
Interior Villages						
Before treatment ...	222	83·3	54	17	19	10
After treatment ...	168	72·6	56	17	16	11
Untreated	51	70·6	91	6	3	0

It is clear that little difference in parasite rates and intensities occurred in the few months of observation.

[These papers do not lend themselves readily to abstraction, and should be studied in the original. Further researches in the field are in progress.]

R. Ford Tredre

RITA, G. & GRAMICCIA, G. Ricerche sulla infezione degli embrioni di pollo con *Plasmodium gallinaceum* (I nota). [**Infection of Chick Embryos with** *P. gallinaceum.*] *Riv. di Parassit.* Rome. 1947, June–Sept., v. 8, Nos. 2/3, 119–24, 2 figs. [12 refs.] English summary (6 lines).

The authors attempted to inoculate 25 embryo chicks from the 9th to the 17th day of incubation. Heavily infected blood was applied to the chorio-allantoic membrane and a small quantity was injected into the vitelline sac. Only two of the chickens, both of the 9th day, acquired an infection. The infection developed rapidly, death occurring on the 5th day after hatching. The parasites, which revealed an abnormal morphology, were readily inoculable to other chickens, the parasites then regaining their normal appearance.

C. M. Wenyon

KNOPPERS, A. T. **Acquired Resistance (Twofold) to Quinine in** *Plasmodium gallinaceum.* [Correspondence.] *Nature.* 1947, Nov. 1, 606–7.

It was recently shown by BISHOP & BIRKETT and by WILLIAMSON *et al.* [this *Bulletin*, 1947, v. 44, 969, 970] that *P. gallinaceum* maintained in chickens

could acquire resistance to paludrine. The present author has obtained similar results, but in contrast to the findings of the latter authors an acquired resistance was also demonstrated in the case of quinine. This result was obtained by inoculation of a 7-day-old chick with 50 million parasites followed by treatment with the minimal effective dose of the drug, given once on the day of inoculation and twice on each of the three following days. Reinoculation of a fresh host was carried out with the blood of a treated animal on the same day each week. After treatment of the chickens with 10 mgm./kgm. of quinine base, in the form of hydrochloride, as in the above dosage schedule, some resistance was apparent after 12 weeks. After a further 16 weeks' treatment with double the dose, the course of the infection was scarcely influenced. The degree of resistance was found by experiment to be twofold. After one passage of the resistant strain through *Aëdes aegypti*, this acquired resistance to quinine was partially lost. The quinine-resistant strain showed no such character towards mepacrine, paludrine, or chloroquine. *J. D. Fulton*

TRAGER, W. **The Relation to the Course of Avian Malaria of Biotin and a Fat-Soluble Material having the Biological Activities of Biotin.** *J. Exper. Med.* 1947, June 1, v. 85, No. 6, 663–83, 6 figs. [36 refs.]

In a previous paper [this *Bulletin*, 1943, v. 40, 825] the author produced evidence that deficiency of biotin lessened the resistance of chickens and ducks to malaria infections. He subsequently found [*Proc. Soc. Exper. Biol. & Med.*, 1947, v. 64, 129] that the plasma of various animal species after hydrolysis with acids or enzymes contains a fat-soluble material designated FSF, having the biological activity of biotin, but differing from it chemically and which is not inactivated by the avidin of egg white. This substance could replace biotin as a growth factor for *Lactobacillus casei*. Its biotin activity has been used to measure the concentration of the substance, possibly a lipoprotein, from which it arises. Its properties suggest that it is concerned with resistance to infection. Chicks infected with *P. lophurae* and ducks infected with the same parasite or *P. cathemerium* were used in these experiments. The various diets used, which were adequate or deficient in biotin, are described. During malaria infections, the changes in concentration of biotin and of FSF in plasma and organs were measured by a biological method with the use of *L. casei*. Free biotin and FSF were measured in untreated plasma ; the difference between that value and the one obtained after hydrolysis gave the value for bound FSF, biotin itself being unbound. The early inhibition of multiplication of *P. cathemerium* in ducks moderately deficient in biotin was paralleled by the deficiency of riboflavin and pantothenate in other malaria infections of chickens and by vitamin C deficiencies in monkeys, being due probably to the absence of a specific growth factor for the parasites. The higher peak of infection finally reached in deficient hosts suggested that another factor was at work, which interfered with some defence mechanism of the hosts, other than leucocytes. The concentration of bound FSF in plasma during infection varied to some extent like that of biotin, but the return to normal levels was longer delayed. Whereas the presence of excess free biotin is not associated with a limitation of parasite multiplication, high levels of bound FSF appeared to be associated with increased resistance to parasite growth. After malaria infections, the biotin content of the livers of deficient animals was reduced. In experiments with *P. lophurae in vitro*, in which the biotin content of the medium varied widely, the rate of parasite multiplication was not affected. The addition of α and β globulin fractions from human plasma having a 2 per cent. concentration of FSF caused haemolysis and degeneration of the parasites. Similar effects have been noted with

fractions of animal plasma. The results support the view that the FSF fraction arises from a substance, probably a lipoprotein, which is associated with resistance to malarial avian infection and acts against parasites and sensitized erythrocytes. *J. D. Fulton*

BLACKWATER FEVER

KOLFF, W. J. with the cooperation of J. VAN NOORDWIJK. **The Artificial Kidney.** 92 pp., 46 figs., 4 plans (1 folding), 1 chart & 5 sketches. [21 refs.]. 1946. Kampen, Holland: J. H. Kok N.V.

It is not improbable that the accumulation of diffusable metabolic products in the blood is a contributory cause of death in acute uraemia. The removal of such "retention products" from the blood stream during the period of acute renal failure might help to keep the patient alive until such time as normal renal function is re-established. This book describes in considerable detail a method of removing such products from the blood by dialysis, by the use of a machine which the author has called "the artificial kidney". Other methods, such as irrigation of the peritoneal cavity and perfusion of isolated loops of gut, have occasionally been tried, with some success. Kolff's method is based on extra-corporeal dialysis of the patient's blood by a method rather similar to that previously described by Abel and his colleagues [ABEL, ROWNTREE & TURNER, *J. Pharmacol.* 1913, v. 5, 275]. The machine consists of a "cellophane" tube 30–45 metres long, wrapped round a rotating cylinder, a portion of which is immersed in rinsing fluid which is a solution of sodium chloride (0·6 per cent.), sodium bicarbonate (0·2 per cent.), potassium chloride (0·04 per cent.) and glucose (1·5–2·0 per cent.). Arterial blood from the patient is passed into the "cellophane" tube and returned, after dialysis, by means of a cannula inserted into the patient's vein. The artificial kidney can deal with up to half a litre of blood at any one time, and large quantities of blood can be dialysed in it in a short period. Thus in one case, 80 litres of blood passed through it in under 12 hours. Kolff has reported the use of his artificial kidney in 17 cases of chronic and acute uraemia. In this series there were 2 recoveries. He has since reported 8 additional cases with 3 more recoveries [*Lancet*, 1946, Nov. 16, 726]. Extra-corporeal dialysis of blood in large volumes appears now to be a practicable proposition provided the apparatus is to hand. As was pointed out in the leading article in the *Lancet* [1946, Nov. 16, 720], Dr. Kolff "has provided evidence indicating that in some cases dialysis may tide the patient over a period of acute renal failure and keep him going until renal function is restored." The technique should be of value in those cases of potentially reversible renal failure which have been called "renal anoxia" [MAEGRAITH, HAVARD & PARSONS (this *Bulletin*, 1945, v. 42, 968)] in Britain, and "lower nephron nephrosis" in America, [LUCKÉ, *Milit. Surgeon*, 1946, v. 99, 371]. It is hoped that one day the opportunity may arise to test this technique in anuric blackwater fever. *B. G. Maegraith*

GOODYEAR, W. E. & BEARD, D. E. **The Successful Treatment of Acute Renal Failure by Peritoneal Irrigation.** *J. Amer. Med. Ass.* 1947, Apr. 19, v. 133, No. 16, 1208–10, 2 figs.

The possibility that death, in acute renal failure of a reversible kind, may be due to the accumulation of substances normally excreted by the kidneys, has given rise to the development of several methods of removing such substances from the blood, and so prolonging life until the kidneys can recover sufficiently

to resume function. One of the techniques which has lately been stressed is based on a method of dialysis of the patient's blood by a machine which has been called the artificial kidney by its designers (KOLFF and BERK, *Acta Med. Scandinavica*, 1944, v. 117, 121), [see also above]. This consists of a "cellophane" tube partly immersed in a solution of sodium chloride, sodium bicarbonate, potassium chloride and glucose. Blood from the patient is passed through this apparatus from a cannula in the radial artery, and back into the body by a cannula into a vein of the foot or forearm. In this way, substances such as excess urea are dialysed.

The present authors have used an alternative method and have utilized the NaCl 8·0 gm.; KCl 0·2 gm.; $CaCl_2$ 0·1 gm.; $MgCl_2$ 0·1 gm.; $NaHCO_3$ 1·0 gm.; peritoneum as the dialysing area. The irrigating fluid contained (per litre), sodium biphosphate 0·05 gm.; dextrose 1·5 gm.; heparin 0·5 mgm.; penicillin 5,000 units, and sulphadiazine sodium 0·1 gm. Catheters were inserted into the peritoneal space and the incision was closed. The irrigating solution was admitted to the peritoneal cavity by a drip method. The average rate of irrigation was 500 cc. per hour for two days, and 300 cc. per hour for the two following days. The technique was tried in a white woman who developed a reaction subsequent to transfusion following a nephrectomy. The reaction was complicated by suppression of urine and rapidly increasing azotaemia. Peritoneal irrigation was instituted 84 hours after the nephrectomy, and continuous irrigation was maintained for 4 days. The azotaemia was rapidly reduced and the urinary output rose from 20 cc. to 240 cc. per day. There was remarkable clinical improvement. The non-protein nitrogen of the blood reached 100 mgm. per cent. within 3 days of the discontinuation of the peritoneal irrigation, but the urinary output steadily rose and the patient made an uninterrupted recovery. The urea content of the recovered peritoneal washings varied from 47 to 53 mgm. per cent. The urine excreted after a resumption of renal function had a urea content of 100–140 mgm. per cent. and a specific gravity of 1010–1012.

[The interest of this case from the point of view of tropical medicine lies in the possible application of such methods to cases of renal failure of the renal anoxic type occurring, for example, in blackwater fever or cholera. It is possible that an artificial kidney of the type described by Kolff and Berk might give more satisfactory results as far as dialysis of the blood is concerned.] [A case of peritoneal irrigation for uraemia after an incompatible blood transfusion is described by MUIRHEAD *et al.* (*Arch. Surgery*, 1947, v. 54, 374). Ed.]

B. G. Maegraith

TRYPANOSOMIASIS

NIGERIA. **Sleeping Sickness Service. Annual Report. 1946.** *Nigeria Rep. on Med. Services for Year 1946.* 22–9. 1947. London: 4 Millbank, S.W.1. [9*d*.]

Abstracted, from a mimeographed copy, in this *Bulletin*, 1947, v. 44, 973-5.

NODENOT, L. Note sur le traitement de la maladie du sommeil par la pentamidine. [**The Treatment of Sleeping Sickness with Pentamidine.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1946, v. 3, No. 2, 215–26. [23 refs.]

Results obtained with pentamidine [presumably the isethionate], in the treatment of sleeping sickness at Bobo-Dioulasso since 1944, may be summarized in the table below, constructed from the author's text.

First series. Followed for 6 to 10 months; some for more than 1 year

Type of case		Pentamidine treatment, i.m.; repeated for 5 doses*	Cases	Possibly cured	No improvement†	Relapsed
Early	Previously untreated	2 mgm/kgm.	76	73	2	1
		3 ,, ,,	4	4		
	Reinfection	2 ,, ,,	2	2		
	Arseno-resistant relapse	2 ,, ,,	3	3		
		3 ,, ,,	1	1		
Late	Previously untreated	2 ,, ,, followed by tryparsamide‡	10	5	5	
	Chemo-resistant§	,, ,, ,,	9	2	7 (6)	

Second series. Followed for shorter periods than the first series.

Early	Previously untreated	4 mgm./kgm.	60	56	4	
Late	Slightly altered c.s.f.**	4 ,, ,,	10	4	6	
		4 ,, ,, ††	3	2	1	
		6 ,, ,,	7	4	3	
		6 ,, ,, ††	2	2		
	Much altered c.s.f.**	4–6 ,, ,, plus intrathecal treatment§§	14	0	14 (6)	
	Chemo-resistant§	4 mgm./kgm.	20	4	16 (2)	
		i.m. plus intrathecal treatment§§	21	0	21 (9)	

*On alternate days for 1st series; daily for 2nd series.
†Number of deaths shown in brackets.
‡Course of 10 intravenous injections.
§Previously uninfluenced by treatment with arsenicals and suramin.
**Details of c.s.f. changes not stated.
††Re-treatment of uncured patients of group immediately above. Treated 1 month after end of previous course.
§§Using 1 per cent. pentamidine, further diluted in c.s.f. in the syringe before injecting. First cases treated with 3 doses of 15 mgm., given after 1st, 3rd and 5th i.m. injections. Later cases treated with 1 or 2 doses of 10 mgm.

The author concludes that a dose of 2 mgm./kgm. pentamidine per injection is hardly sufficient, and 3 mgm./kgm. is recommended. In high dosage the

drug is effective up to, but no later than, the time when the infection begins to involve the central nervous system.

Intrathecal treatment is extremely toxic, and generally aggravates the infection. *E. M. Lourie*

See also p. 201 WOODMAN, **Nutrition of the African in Tsetse-Fly Areas.**

MAZZOTTI, L. Presencia en Mexico de *Triatoma protracta woodi* Usinger y de *Triatoma gerstaeckeri* (Stål). [**Presence in Mexico of** *Triatoma protracta woodi* **Usinger and** *Triatoma gerstaeckeri* **(Stål).**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1947, Mar., v. 8, No. 1, 69–70.

This paper records the finding of *Triatoma protracta woodi* in the State of Coahuila, Mexico. In the same area, specimens of *T. gerstaeckeri* were collected : this species has previously been recorded in the State of Nuevo León in 1941. Both species were found to be infected naturally with *Trypanosoma cruzi*.

The insects were found in nests of *Neotoma micropus canescens*, on which they appear to feed. *H. J. O'D. Burke-Gaffney*

LEISHMANIASIS

LUENGO ARROYO, E., NÁJERA ANGULO, L. & LOZANO MORALES, A. Problema sanitario de la leishmaniosis visceral mediterranea en España. (Ponencía oficial.) [**The Problem of Visceral Leishmaniasis in Spain from the Sanitation Aspect.**] *Kuba.* Habana. 1947, Aug., v. 3, No. 8, 167–77, 1 fig.

Since the report of PITTALUGA and VILÁ of the finding of cases of infantile kala azar in Spain in 1912, some 2,000 cases have been recorded. In the year ending 31st May, 1946, there were 138 noted in 13 Provinces ; the most, 31, in Jaén, next, 28, in Toledo, fewest, one only, in Madrid.

The authors consider the question of geographical distribution (just related), the aetiology, diagnosis and treatment, the epidemiology and prevention. Diagnosis was made on clinical, haematological and serological grounds, such as the globulin tests of Brahmachari, the ureastibamine test of Chopra and Das Gupta, the antimony-formol test of Nattan-Larrier, the sulpharsenol test of Caminopetros, and others, or by the intradermo-reaction or by deviation of complement ; by spleen or marrow puncture. The authors have nothing fresh to add on the subject of treatment. As regards epidemiology they suggest that, besides the dog, the squirrel, *Xerus getulus*, may be a reservoir host.

H. Harold Scott

KIRK, R. & LEWIS, D. J. **Studies in Leishmaniasis in the Anglo-Egyptian Sudan. IX. Further Observations on the Sandflies** (*Phlebotomus*) **of the Sudan.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 869–88, 2 maps & 2 figs. [44 refs.]

The collecting of sandflies in the Sudan by the oiled-paper method has resulted in the finding of 25 species of *Phlebotomus* ; these are listed and the bionomics of some are described.

P. langeroni var. *orientalis* is the only one of the *P. major* group whose distribution is related to that of kala azar in the Sudan. Its occurrence is erratic and variable and may have some bearing on the erratic and variable

occurrence of kala azar. Unpublished observations revealed the "anterior" development of the parasites in gorged females which had fed on a patient with post-kala azar dermal leishmaniasis.

The common outdoor species *P. clydei* bites man in and out of doors. In experiments, the development of flagellates has been observed in one out of forty specimens, but the development was not of the "anterior" type.

The commonest and most widely distributed species is *P. signatipennis*, but it feeds on geckos and seldom or never on man.

P. papatasi readily bites man indoors and has also been observed to bite outside.

The authors have made a special study of the haunts of *Phlebotomus* adults, particularly of holes and cracks in the ground. From observations and trapping experiments, they have accumulated considerable evidence that a vast subterranean environment exists in the Sudan plains, consisting of animal burrows in the sandy parts and of cracks in the heavy clay known as "black cotton soil". These are adult resting places, but whether they are also breeding places is not certain as no thorough search was made for immature stages.

H. S. Leeson

ANSARI, N. Leishmaniose expérimentale à *L. tropica* chez la souris. [**Experimental Leishmaniasis produced in the Mouse by** *L. tropica*.] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 82–6, 4 figs. on 2 pls.

Using a strain of *L. tropica* isolated in culture (N.N.N. medium) from facial lesions of a girl suffering from Oriental sore, the author inoculated 108 young white mice by intradermal, intratesticular and intraperitoneal routes. Intradermal injection at the base of the tail produced in 4 out of 8 mice cutaneous lesions at the site of inoculation, in one case accompanied by visceral infection. Intraperitoneal injection of 22 mice resulted in a generalized infection varying in severity in 17 cases. The most constant positive results were obtained after intratesticular inoculation of 78 mice, 67 of which acquired a generalized infection, while in 6 cases the infection was restricted to the testes. In each of the above series, a number of mice were refractory. The incubation period of experimental leishmaniasis in mice varied from 60 to 90 days. As a rule the mice succumbed to the infection in from 98 to 188 days. The occurrence of parasites, as revealed in smears, varied in different organs and tissues which are arranged in the descending order of frequency as follows: testes, ganglia, spleen, liver, peritoneum, bone-marrow, kidneys, lungs and suprarenal glands. The histo-pathological findings, which are described in detail, can be summarized as follows. At the point of inoculation there appears a granuloma consisting mainly of macrophages loaded with leishmania. The granuloma undergoes secondary necrosis and gives rise to a lesion closely resembling that of oriental sore in man. This localized lesion is followed by a generalization of the pathological process, which spreads to the spleen, ganglia, bone-marrow, liver and lungs, involving the reticulo-endothelial system exclusively, the cells of which are packed with parasites. This process of infiltration, representing a veritable parasitic blockade, is accompanied by proliferation of cells of the reticulo-endothelial system, which is especially marked in the spleen and liver, giving rise to histo-pathological changes resembling those in kala azar. [The paper is illustrated by 3 photographs and one photomicrograph.]

C. A. Hoare

SEAGER, L. D. & CASTELNUOVO, Gina. **Toxicity of "Stilbamidine". A Study of the Effects of Chronic Intoxication.** *Arch. Pathology.* 1947, Sept., v. 44, No. 3, 287–96, 4 figs. [Refs. in footnotes.]

The toxic effects of stilbamidine on animals have been reported by a number of workers [this *Bulletin*, 1940, v. 37, 700; 1943, v. 40, 683; 1945, v. 42, 18;

1946, v. 43, 1029]. The present authors have investigated the histological changes produced by this substance after different dosage schedules in 160 rabbits and 100 mice. Many organs and tissues were studied ; but the changes, chiefly degenerative, were most marked in liver and kidney. Detailed descriptions are recorded for these organs in animals killed at various intervals after drug administration. The nervous system was not investigated. Rabbits were treated subcutaneously with the drug and mice by the same route as well as by stomach tube. The doses ranged from 10 to 100 mgm. per kilo and were given in single or multiple injections. During treatment rabbits lost weight, had diarrhoea and suffered from weakness, congestion of the iris and fall in blood pressure. Attempts to counteract these conditions were not successful. Blood sugar estimations indicated a hyper- or hypoglycaemic condition at different times, those for blood urea nitrogen were inconclusive, while the van den Bergh test became positive after a short time. The chief change in the blood picture was a shift to the left in the leucocyte count ; nucleated red cells were sometimes seen. Mice proved more tolerant of the drug, but changes comparable with those seen in the rabbit tissues were noted. There appeared to be no correlation between dosage and the histological picture.

J. D. Fulton

FEVERS OF THE TYPHUS GROUP

BUSTAMANTE, M. E. & VARELA, G. Distribución de las rickettsiasis en Mexico. (Tifo murino, tifo clásico y fiebre manchada.) [**Distribution of Rickettsial Disease in Mexico. (Murine and Epidemic Typhus and Rocky Mountain Spotted Fever.)**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1947, Mar., v. 8, No. 1, 3–14, 5 maps & 3 figs. [17 refs.] English summary.

The incidence in Mexican States of the three rickettsial diseases in question is discussed and shown in a table. In each case the presence of the disease was established by the isolation of strains or by complement fixation or both.

Murine typhus was found in 18 States and epidemic typhus in 19, which included 12 which also had the murine type. In the States of Durango and Sinaloa, murine typhus and Rocky Mountain spotted fever were both present ; in Coahuila, all three rickettsial diseases were found ; in San Luis Potosi and Vera Cruz, both epidemic typhus and spotted fever were identified ; and the latter was also isolated in Sonora. The distribution of the three diseases, singly and together, are shown in 4 maps, and the mortality from typhus in Mexico between 1931 and 1942 is shown in another map.

In the north and north-east regions of Mexico, *Rhipicephalus sanguineus* was found naturally infected with the virus of Rocky Mountain spotted fever ; on the east coast, the vector was *Amblyomma cajennense.*

H. J. O'D. Burke-Gaffney

RAYNAL, J. H. La rencontre des *Proteus* à l'occasion du typhus de Chang-Hai. [**The Incidence of *Proteus* Strains during the Epidemic of Typhus Fever at Shanghai.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 7/8, 294–304, 1 chart. [11 refs.]

No strains of *Proteus* were isolated from any of the 300 blood cultures made between 1938 and 1945 in Shanghai during the early stages of attacks of fever which were afterwards found to be due to typhus infection.

From animals experimentally infected with typhus rickettsiae, large numbers of heart-blood cultures were made after death ; *Proteus* organisms were isolated

from 10 per cent. of the white mice examined, from 1·7 per cent. of the white rats, and from only one of several hundreds of the guineapigs.

From wild rats, about 3,000 blood cultures were made; only eight strains of *Proteus* were isolated, but 71 strains were isolated from bone-marrow cultures and 146 from urine cultures.

Among the 301 strains isolated in all the above experiments, 17 behaved like *Proteus OX19* in agglutination tests; eight like *P. OXK*, and one like *P. OX2*. An unstated number reacted in a manner suggesting that they belonged to types intermediate between *Proteus vulgaris* and *Proteus X*.

John W. D. Megaw

DE ROSNAY, D. Etude de la moelle osseuse dans le typhus exanthématique. [**The Bone Marrow in Epidemic Typhus.**] *J. Méd. de Bordeaux.* 1947, Oct., v. 124, No. 10, 480.

In 46 cases of epidemic typhus, the author studied specimens of bone marrow obtained by sternal puncture. He states that the myelogram obtained is characterized by changes in the red cell and myeloid systems and particularly by a definite proliferation of reticulo-endothelial and other elements. These changes are early and, the author states, give the myelogram a very characteristic appearance. Nevertheless, he admits that the changes are not specific; but they do indicate a reticulo-endothelial response of an intensity rarely encountered in other infections; hence he considers that they have some diagnostic value in difficult cases.

By means of special staining techniques, such as hot Giemsa or Giroud's application of Macchiavello's method, cellular inclusions may be seen in some reticulo-endothelial cells in marrow smears: these inclusions recall the forms described by GIROUD and PANTHIER [this *Bulletin*, 1942, v. 39, 753] in the lungs of animals inoculated intratracheally with rickettsiae, and named by them homogeneous bodies.

The author is not prepared, however, on a simple morphological similarity alone, to assign a rickettsial nature to the inclusions seen in the bone marrow in epidemic typhus. Nevertheless, as these appearances are not seen in normal marrow nor in persons suffering from other infections, they have a considerable diagnostic value in the haematological study of epidemic typhus.

H. J. O'D. Burke-Gaffney

SANDOR, G. & GIROUD, P. Nature de l'agglutinine anti-typhus du sérum de lapin. [**The Nature of the Anti-Typhus Agglutinins of Rabbit Serum.**] *C. R. Acad. Sci.* 1947, Oct. 20, v. 225, No. 16, 704–5.

The authors have studied the distribution of the anti-typhus agglutinins in the protein fractions of the serum of rabbits inoculated through the respiratory route with typhus rickettsiae.

Three different euglobulin fractions were isolated from the rabbit serum, whereas only two could be isolated from human and equine sera.

One of the euglobulin fractions from each of the above three sera was found to contain the greater part of the anti-typhus agglutinins, but this fraction in the case of the rabbit was not the same as in the case of man or the horse.

For the technical methods employed the original paper must be consulted.

John W. D. Megaw

SUTORISOVA-STOLSOVA, Marguerite. Action sensibilisatrice de l'alexine au cours de l'agglutination des rickettsies. [**The Sensitizing Action of Complement in connexion with the Rickettsia-Agglutination Reaction.**] *C. R. Soc. Biol.* 1947, July, v. 141, Nos. 13/14, 719–20.

The sensitivity of a formol-killed rickettsial suspension used in carrying out the rickettsia-agglutination test was found to be increased two to eight times

by the addition of complement. [In one of the seven tests of which details are given, the rise in the titre was only from 1–40 +++ to 1–40 ++++.]

John W. D. Megaw

GIROUD, P. & JUDE, A. Conservation du pouvoir agglutinant vis-à-vis des rickettsies des sérums typhiques saturés par le *Proteus OX19*. [**Retention of the Rickettsia-Agglutination Potency of Typhus Serum after Absorption with** *Proteus OX19*.] *C. R. Soc. Biol.* 1947, July, v. 141, Nos. 13/14, 721–2.

Agglutination tests were carried out on epidemic-typhus serum and on the same serum after absorption with a suspension of a culture of *Proteus OX19* which had been heated to 100°C. for 60 minutes. The untreated serum agglutinated *P. OX19* at a titre of 1–1,280, whereas after absorption the titre was only 1–80.

In rickettsiae-agglutination tests in which *Rickettsia prowazeki* and *R. mooseri* were employed, the titres with untreated serum were 1–1,600 for both organisms; with the absorbed serum, they were 1–3,200 and 1–6,400 respectively.

Three samples of murine-typhus serum were tested in the same way, and with similar results; the absorption of the *OX19* agglutinins tended to increase rather than diminish the rickettsial agglutinins, so it was concluded that specific differences existed between the Proteus and rickettsial agglutinins.

John W. D. Megaw

HORTOPANU, D. Gangrenele tifosului exantematic. [**The Forms of Gangrene in Exanthematic Typhus.**] *Rev. Stiinţelor Med.* Bucharest. 1947, Jan.–Apr., v. 36, Nos. 1/4, 114–24. French summary.

The author, in Rumania, reports on the presence of gangrene encountered on 25 occasions among 465 cases of exanthematic typhus seen since 1941: he divides these varieties of gangrene into the following three groups, which he regards as being quite distinct, aetiologically, clinically and therapeutically.

1. *Gangrene from thrombo-arteritis obliterans* of the large arterial vessels is seen especially in the legs: it is unilateral and results in necrosis involving almost the whole limb; but it is fortunately rare, and only 2 cases were seen, in persons of 2½ and 19 years respectively.

This condition begins abruptly with violent pain in the affected limb: after 5 to 6 days of ischaemia, signs of dry gangrene appear; the affected part necroses and is completely mummified in 20 to 30 days. The slough separates in a strikingly clear-cut manner from the healthy living tissues, and this contrast is much more marked than in any other form of gangrene. By the time this has occurred, amputation is confined almost to the dividing of bone, which appears stripped of tissue. Perifemoral sympathectomy or section of the lumbar sympathetic (Leriche's method) should be tried, but are only successful in the first 6 to 8 hours. Acetylcholine should be given at the beginning of the ischaemia, although its effects are rarely marked.

2. *Gangrene limited to the extremities* is distinguished from the preceding variety by its causative lesions, which are the ordinary affections of arterioles as seen in exanthematic typhus. These are seen only in the winter, in patients suffering from cold and malnutrition. Unlike (1) above, this form of gangrene begins insidiously and is limited entirely to the extremities, usually the toes. It is bilateral, and sometimes symmetrical. Necrosis is always superficial. Treatment is wholly conservative and surgical intervention is contraindicated in this form.

3. *Thrombo-angeitis obliterans* (Bürger) is regarded by the author as a late complication of typhus, which should be taken into account in making a prognosis.

H. J. O'D. Burke-Gaffney

SMADEL, J. E., SNYDER, J. C., JACKSON, Elizabeth B., FOX, J. P. & HAMILTON, H. L. **Chemotherapeutic Effect of Acridine Compounds in Experimental Rickettsial Infections in Embryonated Eggs.** *J. Immunology.* 1947, Oct., v. 57, No. 2, 155–71, 4 figs. [32 refs.]

During the war, reports were received that Fussgander in Germany had found certain acridine drugs effective in preventing the death of mice experimentally infected with murine typhus. The chief substances tested by the authors were "nitroacridin 3582" and an arsenical salt of this, called "rutenol" [see this *Bulletin*, 1947, v. 44, 1057]. The tests were carried out on groups of embryo chicks infected with one of the following strains of rickettsiae: *Rickettsia prowazeki*, *R. mooseri*, *R. orientalis*, and *Dermacentroxenus* [*Rickettsia*] *rickettsi*. Both of the substances, when injected in suitable doses into the yolk sacs of embryos inoculated with rickettsiae, produced a definite rickettsiostatic effect and a pronounced delay in the death of the embryo.

Unfortunately the ratio between the therapeutic and toxic doses of the drugs was low, 1–2 to 1–4, whereas for *para*-aminobenzoic acid it was about 1–10. The paper, which contains details of a large number of experiments, will be read by all workers on the chemotherapy of the typhus fevers. A useful bibliography with references to 32 articles is appended.

John W. D. Megaw

RAVENEL, S. F. **The Treatment of Rocky Mountain Spotted Fever with Para-Aminobenzoic Acid: a Comprehensive Plan.** *Southern Med. J.* 1947, Oct., v. 40, No. 10, 801–11, 7 charts. [15 refs.]

A detailed description is given of six cases of Rocky Mountain spotted fever in which *para*-aminobenzoic acid (PABA) was given with strikingly good results.

The total daily dosage recommended by the author is 0·5 gm. per pound of body weight for large children; this amount is given in divided doses every two hours; 1·0 gm. per pound is needed for very small children. Every dose is buffered with 10 cc. of a 5·0 per cent. solution of sodium bicarbonate for each gramme of the drug. In exceptional cases the patient refuses to swallow the medicine and gavage is needed. The treatment is kept up till three or four days after the fall of the temperature.

The blood level of the drug should be estimated daily at exactly the same time in relation to the administration of the previous dose; it should be maintained at between 30 and 60 mgm. per 100 cc.; levels above 80 mgm. are risky.

If the total white-cell count falls below 3,000 per cmm. the drug should be stopped. Abdominal distension and delirium are not infrequently caused, but they are rarely of serious importance.

Details are given of the general treatment, which includes:—(1) the preliminary restoration of the fluid and electrolytic balance by glucose in saline given intravenously; (2) maintenance of this balance by fluids with added sodium chloride by the mouth; (3) correction of acidosis, when necessary, by parenteral injections of sodium lactate; and (4) a diet containing abundant proteins and vitamins.

John W. D. Megaw

CAUGHEY, J. E. & DUDGEON, J. A. **"Q" Fever. A Serological Investigation of a Group of Cases previously reported as Primary Atypical Pneumonia.** *Brit. Med. J.* 1947, Nov. 1, 684–5.

An outbreak in which 511 cases of "primary atypical pneumonia" occurred between February and April, 1945, among British and New Zealand troops in

the Naples–Caserta area was described by ADAMS *et al.* [*Bulletin of Hygiene*, 1946, v. 21, 288]. Nearly two years later, sera were obtained from 20 of the 50 persons whose attacks had been specially studied. Nineteen of the 20 sera gave positive reactions to the complement-fixation test for Q fever at significant titres ranging from 1–4 to 1–128. The tests were carried out by Dr. N. H. Topping of the National Institute of Health, Bethesda, U.S.A. ; the antigen used was an Italian strain of *Rickettsia burneti*.

The outbreak, therefore, appears to have been one of Q fever, of which several outbreaks occurring later in the Mediterranean area were closely studied by American workers, and were identified by the isolation of *R. burneti* and by other tests. Abstracts of 11 papers in which these investigations are described will be found in this *Bulletin*, 1947, v. 44, 62–71.

The paper contains a succinct account of the incidence, clinical features, and epidemiology of Q fever in the Mediterranean area, where the disease—though not fatal—caused great concern to the allied medical staffs because of the occurrence of numerous outbreaks in 1944 and 1945.

[Since this abstract was written there has come to hand the September 1947 number of the *Archives of Internal Medicine*, which contains (p. 413) a letter from GROSSMAN, referring to a paper by him in those *Archives* [see *Bulletin of Hygiene*, 1946, v. 21, 572]. This paper was an article " purporting to describe an outbreak of primary atypical pneumonia observed in Italy in 1944 ". On comparing his cases with those of ROBBINS and RAGAN and FEINSTEIN *et al.* [this *Bulletin*, 1947, v. 44, 62, 66], Dr. Grossman now believes that his cases also were those of Q fever.]

John W. D. Megaw

COMBIESCO, D., VASILIU, V. & DUMITRESCO, N. Identification d'une nouvelle rickettsiose chez l'homme en Roumanie. [**Identification of a New Rickettsial Disease in Man in Rumania.**] *C. R. Soc. Biol.* 1947, July, v. 141, Nos. 13/14, 716–17.

In the late winter and early spring of 1947, the author observed several patients whose symptoms suggested that they were suffering from a " new disease ". From the blood of five of the patients, two strains of rickettsiae were isolated by passage, first through guineapigs, and then through chick embryos. Suspensions of blood and organs of the infected guineapigs were still infective after filtration [no details are given of the candles used].

The symptoms were similar to those observed in the various outbreaks of Q fever mentioned in the above abstract, so the authors conclude that the disease was analogous to, if not identical with, Q fever or " Balkan grippe ".

John W. D. Megaw

BARTONELLOSIS

RICKETTS, W. E. **Carrion's Disease. A Study of the Incubation Period in Thirteen Cases.** *Amer. J. Trop. Med.* 1947, Sept., v. 27, No. 5, 657–9.

Much controversy has arisen in the past regarding the incubation period of Carrión's disease, which has been variously estimated as being from a few days to several months. Most of these early studies were made in the absence of cultures for *Bartonella bacilliformis*.

The author studied 13 cases of the disease in different hospitals in Lima, Peru, between 1938 and 1942 : in all, *Bartonella* was demonstrated in the blood, either by culture or direct smear.

All the patients had been healthy, before becoming exposed to *Phlebotomus* in the endemic area. There were two groups. In one, there were seven persons

who had only been in endemic zones for a few hours to three days: this incubation period was thus accurately estimated; it varied from 20 to 23 days in four cases, and in the other three it was 40, 88 to 90 and 100 respectively. Details are given of two such cases.

In the second group of six persons, the incubation period could only be estimated approximately, as the persons remained permanently in the endemic area. In these, the period of incubation varied from 19 to 30 days, indicating that infection occurred during first exposure.

The author discusses the former difficulty in establishing the incubation period of Carrión's disease, which is attributable mainly to the limited number of observations, the lack of reliability of patients' histories, and the varying symptomatology of the disease.

The vague symptoms met with in the initial stage of atypical and subclinical cases are often interpreted by patients as "flu" and "gastro-intestinal upsets". In the present series, the finding of *Bartonella bacilliformis* in blood cultures taken during these "apparently non-specific episodes" made diagnosis possible: in Oroya fever, the marked anaemia and slight jaundice, with *Bartonella* in the peripheral red blood cells, permit of an early diagnosis.

The author points out that the above findings agree with the result of experimental human inoculations. The first made by Carrión himself indicated an incubation period of 21 days: in the second, KUCZINSKI-GODARD observed initial symptoms 17 days after he had inoculated himself.

H. J. O'D. Burke-Gaffney

POMERAT, C. M., FRIEDEN, E. H. & YEAGER, Enid. **Reticulo-Endothelial Immune Serum (Reis). V. An Experimental Anemia in Bartonella infected Rats produced by Anti-Blood Immune Serum.** *J. Infect. Dis.* 1947, Mar.–Apr., v. 80, No. 2, 154–63, 4 figs. [20 refs.]

DENGUE AND ALLIED FEVERS

PAVLOVSKY, E. N. **Pappataci Fever and its Vector.** State Medical Publication. 90 pp., 35 text figs. 1947, Leningrad. [In Russian.] [3·75 Roubles.]

The aim of this book is to provide Russian medical officers with a guide to sandfly fever, which in the Soviet Union is endemic in the Crimea, in Southern Ukraine, Transcaucasia and Middle Asia. A historical introduction, dealing with the achievements of Russian workers in the study of the disease during the last 25 years, is followed by a chapter in which sandfly fever is defined and data are given regarding its geographical distribution, aetiology, course of infection, diagnosis and treatment. Short chapters are devoted to the properties of the virus and to questions regarding susceptibility of lower animals to the infection. The greater part of the book is concerned with various aspects of the epidemioiogy of the disease, particular attention being devoted to the vector, *Phlebotomus papatasi*, the development and bionomics of which are described in some detail. These data are used as a basis for sandfly control, including methods of protection and destruction employed against these insects, which are fully described. The systematic application of these measures for the prophylaxis of sandfly fever has already resulted in a marked diminution of the incidence of infection in Sebastopol. A separate chapter deals with immunity in sandfly fever.

This book, which provides in concise form all the essential information regarding sandfly fever, is a useful addition to the literature on tropical and subtropical diseases.

C. A. Hoare

PLAGUE

PUBLIC HEALTH REP. Wash. 1947, Sept. 12, v. 62, No. 37, 1336–40. **Plague Infection reported in the United States in 1946.**

No human case of plague was reported in the United States in 1946, nor has one been notified since 1943 (except for a laboratory infection in San Francisco in 1944).

During the year, plague infection was found in wild rodents or their ectoparasites from 9 counties of California and 1 county each in Oregon, Kansas and Texas. The proved area of infection in wild rodents in the western United States was extended further east by positive findings in tissues from a prairie dog, and in a pool of fleas from these animals, in Scott County, Kansas.

Details of these field surveys are given in a table : it is emphasized that the reports " are at best, essentially sampling procedures " conducted by some six or seven field units of the U.S. Public Health Service in 12 states. A hunting area in the field usually covers some 5 to 25 miles.

Plague infection was proved during the year in tissue specimens or ectoparasites from species of ground squirrels, chipmunks, field mice, grasshopper mice, white-footed mice, rats, kangaroo rats, prairie dogs and a cottontail rabbit.

H. J. O'D. Burke-Gaffney

HOEKENGA, M. T. **Plague in the Americas.** *J. Trop. Med. & Hyg.* 1947, Oct., v. 50, No. 10, 190–201, 3 figs. (1 map). [Numerous refs.]

At the beginning of this review are a most useful map and a most useful table. The former shows throughout the Americas in differential shading the areas of human and sylvatic plague respectively. In the latter there are set out countries in the American continent where human cases of plague were first reported, the source of original infection, the year in which the last human case was reported and other useful data. Most of the events given in short summaries for the separate countries have already been published. Two factors in the perpetuation of plague in wild rodents are noted for the readers' attention : (1) chronic or latent infection of the rodents, demonstrated especially in squirrels (*Citellus beecheyi*) by organ pool methods ; and (2) lengthened infectivity of fleas for periods such as five months and even 396 days. Some special clinical manifestations are commented on, while therapy is treated under the headings sulphonamides, penicillin, streptomycin and serum. Several new control methods are being developed, among which the rodenticides α-naphthyl thiourea (" Antu "), carbon disulphide and sodium fluoracetate (" 1080 ") have been found efficient. As a pulicide, DDT applied with " 1080 " is probably the method of choice in epidemics. Prophylactic immunization fell into disrepute in Latin America but has again taken its place as a control measure. It appears to have taken the form of a killed vaccine grown on agar at room temperature. Abundant references to the literature for all the countries separately are provided.

W. F. Harvey

BARRETO, J. de B. & DE CASTRO, A. Aspectos epidemiológicos da peste no Brasil. [**Epidemiology of Plague in Brazil.**] *Mem. Inst. Oswaldo Cruz.* 1946, Sept., v. 44, No. 3, 505–27, 2 coloured charts. [28 refs.] English summary.

Epidemiological data which could be usefully comparable have not been available in Brazil for very long. They have, however, increased in usefulness during the years since 1941, when progressive improvement in the prophylactic service has taken place, and especially since 1943. Some of the increase in plague, manifest in 1944 and 1945, may have been due to the more accurate

record of the disease. Laboratory diagnosis has been one of the factors in this accuracy: these laboratories were 6 in 1943 and now number 21. A classification of plague cases was adopted with categories: (*a*) positive, (*b*) suspected and (*c*) negative. Some of the older data were salvaged and brought under these headings, so that tables are presented from about the year 1934 onwards. Plague was first recorded as entering Brazil in 1899. Numerous tables are given by the authors illustrating epidemiological and clinical correlations. The first table is an important one, set out in 3-year periods for incidence: 1934–36, 1,247 cases; 1937–39, 301 cases; 1940–42, 650 cases [shown elsewhere as 660]; 1943–45, 412 cases, revealing a decline coincident with the Federal Government's initiation of a campaign against plague in north-east Brazil—the focal plague area of the country. The principal focus has been Pernambuco with 40 to 50 per cent. of the cases in the triennia investigated. Plague as a whole, and this is a very interesting point, has shown three distinctive periods since its entry. In the first period, 1899–1906, plague attacked the principal ports, to pass in the second period to the cities of the interior. In the third period, which continues to the present day, plague is tending to disappear from the cities and to localize itself endemically in rural zones.

The population of the north-east of Brazil is mainly occupied in the cultivation and disposal of cereal crops, cotton, mandioc and a castor oil crop. These crops are stored in the houses and, together with the accession of dirt, become an attraction and shelter for rodents and their fleas.

In the quinquennium 1941–45, there were 749 cases of plague, for three of which there is no information. Many tables deal with the remaining 746 cases. Treatment was developed on modern lines and the sulphonamide drugs proved their efficacy, while penicillin was discarded. In the tables furnished, care is taken to show that the percentages calculated were tested for statistical significance. Sulphadiazine was administered without plague serum in doses of 12 to 14 gm. daily for the 3 first days, and of 8 to 10 gm. daily on subsequent days. The figures for laboratory diagnosis in the 749 cases, after discard of 78 (10 per cent.) cases where this was impossible, show 342 (51 per cent.) confirmed positive while 329 (49 per cent.) were negative, although these latter were recorded as positive on clinical and epidemiological grounds. Medical opinion expressed disapproval of gland puncture as a method of diagnosis and recommended an increased employment of haemoculture, with inoculation of blood direct into the peritoneum of guineapigs. The method of choice for laboratory diagnosis *post mortem* was digitotomy to obtain bone marrow. This, or gland juice, or blood, was preferably sown in roll-culture sulphite agar and thus despatched to the laboratory.

The vector of major epidemiological responsibility remains in Brazil as elsewhere, *X. cheopis* except in San Paulo (temperate zone) where *X. brasiliensis* took its place. *X. brasiliensis* is found on the rat *R. norvegicus* much more frequently than on any of the 3 subspecies of *R. rattus*. Of all the domestic plague rats, *Mus musculus* was least parasitized by *X. brasiliensis*. For all the species of rodents the relative frequency of *X. brasiliensis* increases with the increase in degrees of latitude, from nil in Fortaleza [lat. 3°S.] (*Mus musculus*, *R. r. frugivorus* and *R. r. alexandrinus*) to 48·3 per cent. in S. Paulo [lat. 24°S.] (*R. norvegicus*). It seems probable that climatic conditions are a major factor in relation to the prevalence of *X. cheopis* and *X. brasiliensis*, and this includes seasonal prevalence. In S. Paulo the period from December to March is the rainy season, and May to August the dry season. Apparently rain and high temperature favour more *X. brasiliensis* than *X. cheopis*. Increase of plague is evident in spring and autumn "following the periods of heaviest rainfall, under temperature ranges between 19 and 26°C. and relative humidity between 66 and 83 per cent."

W. F. Harvey

GIRARD, G. Caractères des cultures secondaires obtenues par l'action du bactériophage sur le bacille de la peste. A propos des mutations du bacille pesteux en bacille pseudo-tuberculeux. [**Secondary Cultures obtained by Bacteriophage Action on Plague and Mutation to the Pseudotuberculous Bacillus.**] *Ann. Inst. Pasteur.* 1947, July, v. 73, No. 7, 642–9, 2 figs.

Argument that *P. pseudotuberculosis* is only a variant or mutant of *P. pestis* continues to make its appearance. Girard's own experience is wholly opposed to this idea. If, however, a bacillus is found which ferments glycerin and can be made to ferment rhamnose, that bacillus if it has been isolated as a plague bacillus becomes of necessity the pseudotuberculosis bacillus (of Malassez and Vignol). That this has been done by obtaining secondary colonies after phage action on *P. pestis* is claimed especially by Russian workers. Only once has Girard had occasion even to record what seems to have been a mutation of the plague bacillus under bacteriophage action. It was in a fatal case of plague treated by bacteriophage ; the organism isolated after death, in sharp contrast to that isolated from buboes before death, produced only lesions of chronic plague in the test guineapigs. It was, however, still a plague bacillus.

What explanation then is to be given of the antinomy ? Girard points out that plague bacilli of sylvatic plague origin do acidify glycerin and if they already possess one of the peculiar characters of the pseudotuberculosis bacillus, it is reasonable to suppose that further deviations from type might, say under the action of bacteriophage, bring about the transformation. Plague strains derived from wild rodents, Russian spermophils of the Steppes, ground squirrels of California and sometimes South African gerbils are the strains in question. We are confronted, perhaps, by two differing groups of bacilli ; the murine, which is the non-deviating plague bacillus, and sylvatic bacilli. Girard contends that extracts or filtrates of plague cultures are toxic for rats and mice whereas those of Malassez's bacillus are not, and that this test might now be put into operation in order to clear up what is still obscure in the epidemiology and prophylaxis of plague. *W. F. Harvey*

LIMA, A. da Costa & HATHAWAY, C. R. Pulgas. Bibliografia, catálogo e animais por elas sugados. [**A Bibliography of Fleas and their Animal Hosts.**] *Monografias do Inst. Oswaldo Cruz.* 1946, Dec., No. 4, 522 pp. 1946. Rio de Janeiro : Imprensa Nacional.

This large monograph comprises first a bibliography of books and papers on fleas, arranged chronologically ; the first work quoted is dated 1544 and the last 1944. This is followed by a catalogue of the fleas of the world, the first part of which is an index arranged according to families, subfamilies, genera and species. The catalogue itself occupies some 240 pages, and for each species or subspecies is given extensive information (with references) on synonymy, and information on geographical distribution and on the species of animals which act as hosts.

This is followed by a section of over 80 pages in which the animal hosts are listed in scientific order, with the fleas found on each species tabulated under that species. A general index to the whole work occupies over 100 pages.

Species are not described, but the work does not claim to be more than a catalogue, and it is, indeed, an admirable compilation which should prove to be most useful for reference. The authors have largely followed the classification of WAGNER, as modified, in relation to the fleas of North America, by EWING & FOX [this *Bulletin*, 1943, v. 40, 841]. For the nomenclature of the mammal and bird hosts the authors have followed well-recognized authorities.

The work that has been put into this volume must have been very great indeed. There are a lot of fleas, and it is a solemn thought that, according to ESKEY [this *Bulletin*, 1939, v. 36, 310] any one of them is a potential vector of plague. *Charles Wilcocks*

MEYERS, F. M. Diagnostische moeilijkheden bij pest. [**Diagnostic Difficulties in Plague.**] *Med. Maandblad.* Batavia. 1947, Aug., No. 13, 242–3.

Difficulty in diagnosis of plague is frequently encountered by the clinician and epidemiologist having insufficient experience. The author instances as one example the case of several members of one family admitted simultaneously. The father had clinically and bacteriologically proved plague. One child had fever with small glandular swelling in both groins which were not typical buboes and were negative on gland puncture ; the second child had moderate fever, was mildly ill and had no buboes. All three recovered. There follows detailed description of two patients admitted as suspicious cases of plague, of whom one proved to be suffering from an anaerobic streptococcus septicaemia and the other from atypical pneumonia, probably due to the Friedländer bacillus. Enlargement of lymph nodes was a striking symptom in both cases and both had a panophthalmia. *W. F. Harvey*

CHOLERA

MONTHLY BULL. MINISTRY OF HEALTH & PUB. HEALTH LAB. SERVICE (DIRECTED BY MED. RES. COUNCIL). 1947, Nov., v. 6, 198–203. **Cholera.** A Note by Medical Officers of the Ministry of Health.

A useful summary of the disease and its control.

CHRONICLE WORLD HEALTH ORGANIZATION. 1947, Oct., v. 1, No. 10, 141–5. **Cholera in Egypt.**

This declaration of international health policy is an important, wise document of precautionary measures against epidemic disease as a whole, although directed against cholera in particular. The statement that, " There is reason to believe that a century ago a similar epidemic could not have been checked," does not perhaps quite imply that it would have been checked in this century. A note of caution is sounded against measures of panic instituted in the name of precaution, even if they are only overprecaution, such as the complete closure of frontiers. In that example, much would depend on the type of frontier and the possibility that " it would only provoke clandestine violation " and thus promote the very occurrence legislated against. The argument, of course, can be applied to nearly all prohibitions if they can be, or are, evaded.

All sanitarians are anxious to put into force immediate measures to counter immediate public dangers and the summarized list of commands here set out, twenty-eight in all, should be a very valuable guide in any communicable epidemic. It follows the usual lines and will, doubtless, be transcribed and put into practice by responsible authorities. The summary may be still further abbreviated as : (1) Isolation and observation of patients, contacts and local inhabitants. (2) Accelerated and enforced sanitary measures for disposal of refuse and dejecta. (3) Active and continued disinfection of dwellings, food and water. (4) Prohibitions on congregation and traffic of people, on the use of suspect or non-disinfected food and water, on the use of public conveniences

or drainage systems with free communication into distributive water. (5) Immediate inoculation of contacts and mass inoculation of entire populations at risk.

Discussions have taken place among experts with all the evidence of friendly international cooperation. Most of the opinions expressed have been on traditional lines. [One would have welcomed also some opinion that the opportunity should be taken, internationally, to investigate :—traditional views for their validity, their dependence on unconscious selection of data, their statistical significance ; the question of endemicity ; prescribed measures, not only for their efficacy but their degree of efficacy ; by definitive search the existence of negative instances ; and the use of some form of alternate case method. If sanely presented, such suggestions might escape the accusation of being inhumane and qualify for statistically-scientific status.]

Conventions which are now recommended are : "(*a*) surveillance for travellers adequately protected by vaccination ; (*b*) surveillance and medical examination for those who have not been vaccinated."

These are very reasonable, and would presumably be accompanied by the recommendation for continued research into their foundation.

W. F. Harvey

i. LANCET. 1947, Nov. 8, 694–5, 1 chart. **Epidemiology of Cholera.**

ii. ABDOU, S. **The Cholera Epidemic in Egypt. Mode of Spread.** *Lancet.* 1947, Nov. 8, 696–7, 2 figs.

iii. LANCET. 1947, Nov. 8, 697–8. **Anti-Cholera Measures in Egypt, from a Correspondent in Egypt.**

i. With the appearance of epidemic cholera and its threat to the valley of the Nile and the deltaic area, attention is inevitably directed to India, the traditional home of cholera. The Yangtse valley is too far distant to be considered in this connexion. It is not, however, the Ganges valley which is mentioned in this discussion, but the Punjab, where epidemic cholera started on August 15, 1947. The epidemiology of cholera was dealt with in a general and Indian sense by Sir John Taylor at a recent meeting of the Royal Society of Medicine. Upwards of 200,000 persons die of cholera in India every year. The routes of spread from this focus are : (1) *via* Afghanistan to Persia and S.E. Russia, not now a major danger ; (2) *via* Iraq, Syria and Turkey to the Mediterranean ; and (3) by the Red Sea to Egypt. Egyptian cholera is, or has been, linked with the annual pilgrimage to Mecca, but effective quarantine measures have, since 1912, eliminated this source of infection. Cholera patients and cholera contacts are probably the main source of cholera infection, apart from short-distance transmission extracorporeally, and both patients and contacts may excrete vibrios for about five days. The Egyptian epidemic, having reached a peak, should, like other epidemics, prophesies Sir Leonard Rogers, now die down though with some prospect of recrudescence next year. Among public health measures to be imposed in Egypt was, said Dr. Melville Mackenzie, surveillance "on air passengers who had spent nights in Egypt." The rapid advance of air travel and the shortening of time involved seem to demand a significant alteration of quarantine measures, based as they have been upon an incubation period for cholera of five days and an average excretion of vibrios also for five days. Identification of the cholera vibrio was dealt with by Mr. Bruce White and especially of the three types of cholera vibrio, described as "original, intermediate and variant." These variants or sports are transmutable, but not in the course of infection. Transmutation of non-pathogenic vibrios is another question altogether.

ii. Dr. Abdou deals with the course of the present epidemic in Egypt and contributes most interesting details. It started in El Korein, a town of 15,000 inhabitants in the date-growing province of Sharkieh. Perhaps the most important point to note regarding the population is that it has been augmented by some 6,000 immigrants settled there to work in British camps, and by 9,000 others during the date season. No correlation between the present epidemic and the British forces is admitted by the authorities. In connexion with the spread of the epidemic there is mentioned the case of an old woman in El Korein who contracted cholera and who sent her grand-daughter to her mother in Demouh with a present of dates on October 1. The mother developed cholera and so the epidemic received its further impetus into the province of Dakahlieh. Dates and escaping settlers are incriminated as the agents of spread of cholera. It seems to have been proved that the cholera vibrio cannot live in compressed dates, but that it can live for some time on the skin of ripe dates. It is interesting to find a brief reference to the report of a medical commission sent to investigate the first cases of cholera in this region in the 1895 epidemic :—" Clinical and bacteriological examination has proved that the disease prevailing at El-Salhieh is a gastro-enteritis due to the over-eating of dates and salted fish. . . . " [Experience of cholera outbreaks in the riverine delta of Iraq during the date season in the first world war may be recalled.]

iii. In this Egyptian epidemic, the main water supplies do not appear to have played any part in the spread, but the badly constructed shallow wells have been a factor in so far as the disease has been water-borne. It is because of their better water supplies and hygienic conditions that Cairo, Alexandria and the other big cities have largely escaped infection. " The number of reported cases, including suspects from Sept. 23 to Oct. 21 reached 8,308 with 3,230 deaths (39 per cent.)". It seems to be too early yet to judge of the value of the newer methods of treatment employed, but restoration of the depletion of water, and presumably salt, is regarded as a sheet anchor. The prophylactic value of vaccination " seems to be fully confirmed " while " experience with sulphonamides has been on the whole disappointing ". " A huge campaign is being carried out to vaccinate the whole population of Egypt ". A vigorous use of DDT was instituted to combat the fly menace. It may be expected that still closer analysis of this epidemic will receive publication and may help to clear up the constantly recurring problems of distant transmission, endemicity and the variant vibrios. *W. F. Harvey*

BLASS, Judith. Sur le métabolisme du glucose par les vibrions non proliférants. [**Metabolism of Glucose by Non-Proliferating Vibrios.**] *Ann. Inst. Pasteur.* 1947, Sept., v. 73, No. 9, 885–99, 4 figs. [13 refs.]

In summary the findings for washed, non-proliferating vibrios, suspended in buffer phosphate (M/15) at *p*H 8 are :—(1) The speed of fermentation of glucose measured by the variation of *p*H and of titratable acidity for time in parallel with the variation in glucose consumed, is more feeble in aerobiosis than in anaerobiosis. The difference is especially marked with active aeration. (2) Qualitative tests have confirmed the presence of CO_2, acetic acid, formic acid, lactic acid and alcohol. The succinic acid found among the products of fermentation of glucose by the cholera vibrio are derived mainly from the asparagin and peptones of the medium. (3) Quantitative studies have shown that the ratio, CO_2 produced to glucose consumed, is variable under aerobic and anaerobic conditions of growth. It could not be used to differentiate between the *Vibrio cholerae* and the *Vibrio El Tor* except under rigorously standardized conditions. *W. F. Harvey*

GALLUT, J. Sur l'utilisation du glucose par le vibrion cholérique en aérobiose forcée. [**Utilization of Glucose by the Cholera Vibrio under Forced Aerobiosis.**] *Ann. Inst. Pasteur.* 1947, July, v. 73, No. 7, 650–59, 2 figs. [13 refs.]

Gallut pursues his researches [this *Bulletin*, 1943, v. 40, 910 ; 1946, v. 43, 129 ; 1947, v. 44, 421 and 660] on the metabolism of the cholera vibrio and finds that both the toxic fractions are liberated in non-aerated glucose media. It follows that the utilization of glucose by combustion instead of fermentation has no effect on the liberation of toxin. His researches lead him to insist that the differences in the morphology of the vibrios as well as in their chemical structure require continued study before concluding that cultivation under the restraint of aerobiosis in glucose media will lead to increase in antigenic power, that is, to an improved cholera vaccine. The argument is, in fact, for study of the natural biological mode of growth of the cholera vibrio as it occurs in the human intestine, with a view to obtaining effective antigen for immunization.

Gallut finds advantage in using heated agar-grown, aerated-culture, suspension [LINTON and JENNINGS : this *Bulletin*, 1945, v. 42, 378, 379] as well as ordinary peptone water culture for comparison of the chief characteristics of his cultures of the cholera vibrio in glucose media, which are strictly aerobic and non-aerated. These characters are set out in a table.

Some characters of the cholera vibrios according to the method of cultivation (24 hours at 37°C.)

	Culture in Buffered Glucose		Culture in Normal Peptone Water	Emulsion of Culture on Agar (Vaccine)
	Aerated	Normal		
E_H limits (mv.) :				
Upper	+81	+150	+150	—
Lower	+42	−200	−250	—
*p*H limits :				
Upper	8·32	8·0	8·2	8·0
Lower	7·05	6·6	7·6	—
Vibrios per cubic centimetre :				
Milligramme (dry)	0·909	0·240	0·914	0·750
Number × 10^6	4·848	1·280	4·874	4·000
Glucose broth (per cent.)	1·48	0·33	—	—
Total nitrogen (mgm. per cc.) :				
Fluid	0·109	0·150	3·523	—
Vibrios	0·063	0·024	0·109	0·106
Nitrogen content of vibrios (per cent.)	7·0	10·1	13	15
O antigen (mgm. per cc.)	0·137	0·030	0·065	0·035
O antigen content of vibrios (per cent.)	15·0	12·5	7·1	4·6
Nitrogen content of O antigen (per cent.)	2	—	5	5

This work confirms the adaptability of the cholera vibrio, which is normally a facultative anaerobe, to a strict aerobiosis during the phase of growth. It can utilize glucose in aerated media at *p*H 7 to 8 and at slightly positive

oxidation-reduction potential (E_H O at 100 mv.) by combustion instead of fermentation. *W. F. Harvey*

See also p. 160 GOODYEAR & BEARD. **The Successful Treatment of Acute Renal Failure by Peritoneal Irrigation.**

BURROWS, W., MATHER, Adaline N., ELLIOTT, Marian E. & HAVENS, Isabelle. **Studies on Immunity to Asiatic Cholera. III. The Mouse Protection Test.** *J. Infect. Dis.* 1947, Sept.–Oct., v. 81, No. 2, 157–74. [30 refs.]

In newer methods of measuring degrees of immunity, actual protection is expressed in terms of the proportionate survival of the test animals. The old measure of agglutinin titre is no longer favoured as a real index of the efficiency of vaccine or of serum. Guineapigs are costly when large numbers have to be used and it seems reasonable to make trial of the mouse ; yet mice are relatively resistant to the intraperitoneal inoculation of cholera vibrios in broth or saline suspensions. The incorporation of commercial granular mucin in the inoculum has, however, proved successful in overcoming the resistance of mice. The present experiments, which are very completely controlled and will be a source of reference for workers in the subject, must be read in entirety.

As the passive protection test was more useful than the active, it has been studied in greater detail. Vibrios for inoculation were maintained by weekly subculture on blood veal infusion agar and preserved frozen or in lyophilized culture ; for inoculation they were measured as dry weight (2,000 million= 1 mgm.). Mice were inoculated intraperitoneally from suspensions of 24-hour culture at a concentration of 8 to 14 mgm./ml. and in a dose of 0·2 ml. of the dilutions made from it. The mice were observed after the challenge inoculation for 72 hours ; but only deaths up to 48 hours (which were less erratic than those up to 72 hours and showed sharper end-points) were taken into account in calculating LD_{50} doses.

In the passive protection test, the mice were challenged 6 to 24 hours after intraperitoneal inoculation of the rabbit immune serum. It was not worth while using a normal serum control and the number of LD_{50} doses used was found from the ratio of the LD_{50} of immunized mice to the LD_{50} of untreated mice.

An important pronouncement is that " in a sense the fatal infection of the mouse with cholera vibrios suspended in mucin is a highly artificial one, and it is not unlikely that the ' virulence ' of many common saprophytic [? vibrios] can be similarly enhanced." This is due, in part at least, to the amount and toxicity of bacterial substance of the proliferating bacteria. The most important findings of this very technical paper are that : (1) A standard dose increase or " fold increase " method of titration is not practical, but the protective titre of antibody can be expressed as ratio of the LD_{50} dose for immune mice to that of the control normal mice within reasonable limits. (2) Only a 100-fold difference in protective titre was significant ; a 10-fold difference was not. (3) Protective antibody may be in part anti-endotoxic, and is not necessarily identical with O agglutinin. Little or no justification is found for drawing a close analogy between the experimental infection and human cholera. In the former there is generalized bacteraemia ; in the latter, there is a condition localized to the bowel with only minor and rare invasion of the tissues. *W. F. Harvey*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

NELSON, E. C. **Alcoholic Extract Medium for the Diagnosis and Cultivation of** *Endamoeba histolytica.* *Amer. J. Trop. Med.* 1947, Sept., v. 27, No. 5, 545–52.

A new medium for cultivating *Entamoeba histolytica* is described. It consists of an alcoholic extract of chopped tissue (guineapig liver, cat intestine, egg yolk or almost any animal tissue), in the proportion of 1 part tissue to 9 parts of 95 per cent. alcohol. The spirit is driven off by warming on a water-bath, and the residue is then mixed with melted 2 per cent. agar buffered at *p*H 7·4 in 0·5 per cent. saline. (The agar solution is in the proportion of two to one of the alcoholic extract.) The tubes are put up in a steep slant and an overlay solution of 0·5 per cent. saline, buffered at *p*H 7·4, is added to each tube. Finally a loopful of rice starch is introduced into the medium at the same time as the inoculation.

A lump of infected faeces, the size of a pea, is placed in the tube, and subculture is made after 24 to 48 hours. Most intestinal protozoa grow in the first culture, but *E. histolytica* is the only parasite which survives in the later ones. The culture can be maintained for many months or years by weekly subinoculation.

The method can be employed as a routine diagnostic procedure, and gives better results than the direct methods. *P. C. C. Garnham*

SCHNEIDER, R. F. & SHIELDS, G. W. **Investigation on the Transmission of** *E. histolytica* **by Cockroaches.** *Med. Bull.* New Jersey. 1947, Oct., v. 7, No. 2, 119–21.

The authors, working in Talara, Peru, made cultures of the legs and intestinal contents of 100 cockroaches (species not identified) in a search for viable cysts of *Entamoeba histolytica.* They used *Entamoeba* medium (Difco), to slants of which were added before use a mixture of 1 part of human serum in 6 parts of saline, sufficient to cover the surface : a 5 mm. loop of rice powder was added to each tube. After incubation at 37°C. for 48 hours, the "rice serum" was examined for the presence of *E. histolytica.*

No *E. histolytica* were found in specimens from the legs of the cockroaches, they were found in 7 per cent. of the cultures from the intestinal contents.

The authors conclude that food and utensils can be contaminated by viable forms of *E. histolytica* from the faeces of cockroaches : and that the common cockroach can be incriminated as a carrier of *E. histolytica* in Peru.

H. J. O'D. Burke-Gaffney

RITA, G. Contributo allo studio della sierodiagnosi nell'amebiasi. [**Serodiagnosis of Amoebiasis.**] *Riv. di Parassit.* Rome. 1947, June–Sept., v. 8, Nos. 2/3, 113–18. English summary.

With an antigen prepared from blood and mucus of a case of acute amoebic dysentery by addition of seven volumes of alcohol and filtering after keeping at 45°C. for fifteen days, complement-fixation tests were carried out on 63 cases of amoebiasis. A positive result was obtained in 92 per cent. of the cases. It was found, however, that the antigen reacts with Wassermann-positive sera, and therefore negative sera are alone of value in the amoebiasis tests.

C. M. Wenyon

RUDOLPH, A. M. & BRAUDO, J. L. **Amoeboma of the Large Bowel with a Review of the Literature.** *Clin. Proc.* Cape Town. 1947, Sept., v. 6, No. 7, 287–91, 2 figs. [12 refs.]

BRAS, G. Amoebiasis van de vagina. [**Amoebiasis of the Vagina.**] *Med. Maandblad.* Batavia. 1947, Sept., No. 14, 260–61.

The English summary appended to the paper is as follows :—

" Description of amoebiasis of the vagina, the portio uteri and the left labium majus in a 20 year old Javanese woman in a state of cachexia due to nutritional deficiency and intestinal amoebic dysentery."

SHRAPNEL, B. C. **Oral Emetine in the Treatment of Intestinal Amebiasis.** *Amer. J. Trop. Med.* 1947, Sept., v. 27, No. 5, 527–44.

The drug used in this study was emetine hydrochloride, prepared by Eli Lilly Co., enclosed in " enseals ", or enteric-sealed tablets, administered orally. Each tablet contained one-third of a grain of alkaloid, designed to release emetine into the lower bowel approximately 3–4 hours after ingestion, thus avoiding the emetic effect of its presence in the stomach and upper intestinal tract. A total of 30 cases of intestinal amoebiasis were treated in this series, in age groups ranging from seventeen months to 66 years. These comprised acute and chronic dysenteries, as well as " carriers ".

No selection of cases was made, except that none was included if emetine hydrochloride subcutaneously had already been begun.

The standardized dosage schedule was as follows :—

Children : One tablet ($\frac{1}{3}$ grain) orally, three times daily for 12 days. Total, 12 grains of emetine.

Adults : Two tablets ($\frac{2}{3}$ grain) orally, three times daily for 12 days. Total, 24 grains of emetine.

It was suspected that some tablets might pass unchanged through the intestinal canal, and this was found true in two cases, in which tablets were seen in the rectal lumen during a proctoscopic examination.

The routine observed comprised daily examination and culture of stools, urine examinations, blood measure readings, complete blood counts every three days and proctoscopic examinations, before and after treatment.

The children, varying in age from 15 months to 9 years, comprised two cases of acute dysentery, two chronic and one carrier cases. All presented the picture of secondary anaemia and harboured other intestinal parasites, particularly helminths. They were given vermifuges and purges in addition to oral emetine. One who was critically ill, and whose haemoglobin percentage was less than 10 per cent., required two blood transfusions.

None of the patients vomited or showed toxic manifestations during emetine treatment. The amoebae disappeared between the third and fifth days. Moderate diarrhoea, with pus cells in the faeces, was checked by sulphaguanidine in one case. A noteworthy side effect was the expulsion of large numbers of *Trichuris trichiura* in two patients as the result of oral emetine.

Twenty-five adults aged from 18 to 66 years were treated with two tablets of emetine three times daily for 12 days. They comprised 6 cases of acute dysentery, 13 of chronic and 6 of the " carrier " state.

Toxic symptoms were absent. Diarrhoea in the acute cases subsided and the number of stools was reduced to 2 to 3 daily ; abdominal cramps and tenesmus likewise subsided. Trophozoites of *E. histolytica* had disappeared on the third day, but cysts were found as late as the sixth.

Amoebic ulcerations of the rectum underwent steady healing. In one patient, residual ulcers responded to sulphadiazine.

The author re-examined 24 of 30 cases after a lapse of 2–9 months.

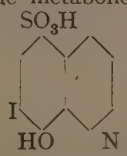
The five children were re-examined 4 to 8 months after treatment. All appeared cured. The blood picture showed marked improvement of the secondary anaemia. Nineteen of the twenty-five adults were followed up for

two to nine months. There was only one failure in this series. All expressed themselves as feeling quite well. No cases of extra-intestinal amoebiasis were encountered.

It is claimed that, though the present series is small, oral emetine, in the form employed, is easy to administer, does not produce toxic symptoms, and gives effective results. *P. Manson-Bahr*

ALBRIGHT, E. C., TABERN, D. L. & GORDON, E. S. **The Metabolism of Chiniofon using Radioactive Iodine.** *Amer. J. Trop. Med.* 1947, Sept., v. 27, No. 5, 553–60, 6 figs.

This elegant piece of work deals with the metabolic fate of chiniofon, (8 hydroxy-7-iodo-quinoline-5-sulphonate)



which has been widely used in the treatment of amoebiasis. In the sample used, stable iodine was replaced by radioactive iodine-131, with a half life period of 8 days, and details of its preparation are given. Radioactivity was measured by means of a Geiger-Muller counter, with a uranium preparation as standard, and data were checked against a known weight of radiochiniofon. The drug was given orally to seven fasting subjects, none of whom had amoebiasis, in single doses of 100 to 300 mgm. so that 0·5 millicurie of radioactivity was not exceeded. Blood was collected up to 8 hours after administration of the drug, and urine and faeces were collected for 2 and 7 days respectively. After the blood was freed from protein, measurements showed that activity was maximal 2 hours after ingestion and declined gradually to a negligible level in 8 hours. Part of the activity was due to iodide formed by degradation of the drug. In the thyroid region, activity was noted for approximately one day. The urine was separated into two fractions by chemical means, one having all the activity of chiniofon and iodide derived from it, and the other that of radiochiniofon alone. The amount of chiniofon excreted in urine and the extent to which it was degraded could thus be ascertained. A marked excretion occurred during the first three hours after ingestion and gradually tailed off, the total voided during the period of observation being about 12 per cent. of the administered dose, of which 7·4 per cent. was unaltered chiniofon. The amount of iodine split from the parent substance increased as time went on. For the examination of faecal specimens, the samples were dried at 85–90°C. for 24 to 48 hours and an aliquot of 5 mgm. of the powder obtained was used for measurement of radio-activity. The amount recovered in faeces varied from 50–60 per cent. of the dose given. When added to that from urine, the total excretion was approximately 70 per cent. of the total dosage. The authors suggest that the incomplete recovery is due to failures in technique rather than to storage in the body. It is clear from the results that absorption of chiniofon does occur fairly rapidly to the extent of 12·9 per cent. of the administered dose, but clinically significant blood levels are not attained. *J. D. Fulton*

PRAMANIK, S. **Balantidiasis.** [Correspondence.] *Brit. Med. J.* 1947, Nov. 15, 794.

Referring to SHUN-SHIN's article on the treatment of balantidial dysentery [this *Bulletin*, 1948, v. 45, 84] the author has administered $\frac{1}{6}$ grain (11 mgm.) of biniodide of mercury intramuscularly to a patient suffering from this disease.

The illness had lasted for three months ; as many as 20 to 30 stools being passed a day. Four days later, the stool examination was negative but the injection was repeated. Two subsequent examinations were negative, the patient then reporting the passage of two or three stools per day. *C. M. Wenyon*

RELAPSING FEVER AND OTHER SPIROCHAETOSES

KERVRAN, P. Recherches sur la sensibilité du poulet à *Spirochaeta duttoni*. Absence d'immunité de l'oiseau infecté contre *Spirochaeta gallinarum*. [**Researches on the Susceptibility of the Fowl to** *Spirochaeta duttoni*. **Absence of Immunity against** *Spirochaeta gallinarum* **in Infected Birds.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 5/6, 152–5, 2 charts.

Using a strain of *Spirochaeta duttoni* originally isolated from a case of relapsing fever at Dakar, the author studied the behaviour of this spirochaete in fowls.

It was found that fowls varying in weight from 525 to 1,400 gm., when inoculated intraperitoneally with the blood of a rat containing this organism, showed a rise in temperature on the 4th day, associated with the presence of very numerous spirochaetes in the circulation for one to two days. With the use of blood containing visible spirochaetes it was possible to maintain the strain by passage in fowls.

The organism does not persist in the brain of the fowl and even in the blood seems to lose its infectivity for the white rat.

Seven fowls infected 3 to 5 months previously with *S. duttoni* were inoculated with *Spirochaeta gallinarum* and all showed numerous spirochaetes in the circulation, but recovered from the infection. *E. Hindle*

LEVADITI, C. & VAISMAN, A. Effets virulicides de la streptomycine dans l'infection récurrentielle de la souris (*Spirochaeta duttoni*). Comparaison avec la pénicilline. [**Action of Streptomycin in Experimental** *Trep. duttoni* **Infections in Mice compared with that of Penicillin.**] *C. R. Acad. Sci.* 1947, Oct. 27, v. 225, No. 17, 769–71.

The authors found that subcutaneous administration of 5,000 units of streptomycin daily for 6 days sterilized the blood of mice which had been inoculated intraperitoneally with blood rich in *Trep. duttoni*. The spirochaetes were absent from the blood of the mice during the 20 days of observation, but appeared in that of control untreated animals on the day after inoculation [and presumably remained there]. Furthermore, brain substance from these treated mice failed to infect clean mice on intraperitoneal inoculation. The authors had already shown [this *Bulletin*, 1947, v. 44, 718] that large doses of penicillin, administered subcutaneously, failed to destroy the residual infection in the central nervous system of mice with long-standing *Trep. duttoni* infections: in the present experiments, they were able to show that in mice infected for 58 and for 94 days, administration of a total of 30,000 units of streptomycin subcutaneously prevented infection of clean mice by means of brain substance from these treated mice in from 62 to 78 per cent. of cases. The brains of untreated control mice remained virulent. Mice infected for 103 days were treated with 160 units of streptomycin daily for 12 days by the intracerebral route ; brain substance, passaged 15 days after the beginning of treatment, failed to infect clean mice, but that of the untreated controls remained virulent.

In concluding that streptomycin, like penicillin, sterilized both the blood and the brain in mice infected with *Trep. duttoni*, the authors point out that, while

penicillin was inactive against residual central nervous infections in mice when given subcutaneously, streptomycin produced a partial sterilization of such residual infections by this route and a total sterilization when given intracerebrally.

They suggest that either streptomycin penetrates the nervous tissues more readily and more intensely than penicillin, or that the residual cerebral infection is more resistant to the latter antibiotic than it is to streptomycin ; investigation of these hypotheses is being carried out. *H. J. O'D. Burke-Gaffney*

HALAWANI, A. **On the Transmission of Relapsing Fever in Egypt.** *J. Egyptian Pub. Health. Ass.* 1946, Nov., v. 21, No. 8, 183–90.

The author discusses the classification of relapsing fever and describes the results of examination of lice, ticks, bugs, fleas and blood-sucking flies during the epidemic of relapsing fever in Egypt in 1945 and 1946.

He notes that body-lice, head-lice and their developmental stages are the chief vectors of relapsing fever in Egypt.

Spirochaetes were found in the coelomic fluid of a few bugs collected from houses : feeding experiments indicated that the spirochaetes were capable of surviving in the coelomic fluid, but they were not found in as large numbers as in the case of lice.

No ticks were found in any of the Egyptian houses examined, nor were fleas found to harbour spirochaetes. *H. J. O'D. Burke-Gaffney*

OMAR, M. El S. **Reinfection in Louse Borne Relapsing Fever.** *J. Egyptian Pub. Health Ass.* 1946, Nov., v. 21, No. 8, 191–4.

An account of three cases.

IVAN, I. M. & ILIESCU, G. A. Contributiuni la studiul elementelor figurate ale sângelui periferic şi organelor hemato-poetice, in febra recurentă Europeană. [**Study of the Peripheral Blood and Haemopoietic System in Relapsing Fever.**] *Rev. Stiinţelor Med.* Bucharest. 1947, Jan.–Apr., v. 36, Nos. 1/4, 76–95, 3 figs. [23 refs.] French summary.

OMAR, M. El S. **Rare Complications of Louse Borne Relapsing Fever.** *J. Egyptian Pub. Health Ass.* 1946, Nov., v. 21, No. 8, 195–200.

The author records the study of 6,921 cases of louse-borne relapsing fever during the epidemics of 1945 and 1946 in Egypt.

The commonest complication was abortion (92 per cent. of pregnancies) : the next commonest was bronchitis (8·6 per cent. of cases). An imposing list of other complications is given and observations are made on twelve of them.

H. J. O'D. Burke-Gaffney

AUBIN, H., GACHKEL, ZANGERLIN, Mme. & GALLO, M. Les troubles mentaux dans la fièvre récurrente. [**Mental Manifestations of Relapsing Fever.**] *Algérie Méd.* 1947, May, No. 5, 408–16.

Relapsing fever was very prevalent in North Africa in 1944–45–46. The observations under review deal with the neurotropic effects of infection with *S. obermeieri*. The nervous types of the disease are classified as follows :—

(A) *Confusional.*—A certain amount of mental confusion is common, but in some cases a severe confusional syndrome, and not merely a temporary state, was observed, the patients being in a condition of extreme prostration, with no perception of time or surroundings, unable to understand questions or to answer coherently. This form can result in acute delirium accompanied by terrifying

dreams and may show sudden and violent exacerbations. In one case (a Mahommedan Algerian) attempts to commit suicide by throwing himself out of the window were noted; these were caused, apparently, by dreams of a terrifying nature. In some instances a form showing very severe prostration, usually ending fatally, was observed. Usually in confusional cases an anxiety state was present.

(B) *Psychical.*—Maniacal forms are common and may occur as a primary manifestation or follow on a purely confusional state, on one of confuso-mania, or on confusion accompanied by an anxiety complex. In one instance (a young soldier), confusional symptoms appeared at the time of the second febrile attack, improvement occurring towards defervescence when a typical maniacal state suddenly supervened. This patient recovered after 5 " electric shock " treatments. In another case (an Algerian) mania, accompanied by grandiose delusions, showed itself before the onset of pyrexia and improvement only occurred after 5 months. Irritability and impulsiveness, especially amongst natives, are other important symptoms in this type, a few electric shock treatments usually suffice to bring about cure.

The depressive form is very rare, having only been seen in one instance, and then following on a confusional state.

(C) *Protracted types.*—Most writers hold that such types are rare, and chronic forms have not been noted. The authors report a case in a Spaniard who became stuporose at the commencement of pyrexia, appearing to have no realization of his identity. After 7 months he recovered use of his speech, admitting having auditory hallucinations; later a diagnosis of paranoia was confirmed. This condition is now of 2 years' standing.

The authors describe several cases showing that mental disorder may become chronic, in some cases ending in actual insanity. " Electric shock " treatment appears to be of benefit in certain instances. Various types, religious mania, delusional and hallucinatory forms are described in some detail.

The time of appearance of psychoses is variable and not necessarily in the " precrisis " of the first febrile attack. Mental symptoms were observed during the incubation period before any signs of infection appeared, and early psychotic forms may develop into mania long after disappearance of signs of infection. It is impossible definitely to separate primary psychoses from those due to the infection.

During the actual attack, confusional conditions with dreams and an anxiety state are most common, but, as noted, the first appearance may often be in the apyrexial phase with absence of spirilla in the blood, and hence one difficulty in diagnosis.

During convalescence mental symptoms tend to appear in more or less atypical forms—delirium with sudden onset and return of pyrexia—psychological troubles of a trivial nature, perhaps delayed for several weeks or months after cessation of pyrexia.

A history of various chronic infections or intoxications is often found, especially alcoholism, which in some cases gives rise to a syndrome resembling delirium tremens, and syphilis. Five patients showed positive Wassermann reactions; one of these, after an attack of relapsing fever, developed a mental syndrome of continued amnesia and puerility, followed by signs of a tabetic type and a spasmodic paraplegia (syndrome of Guillain and Thaon).

[Some authorities hold that relapsing fever does not give a positive W.R. in the blood, others hold a contrary view.]

[Possible mental complications in relapsing fever are worth bearing in mind from a medico-legal aspect in regions where this disease is prevalent.]

C. F. Shelton

EL-RAMLY, A. H. **Three Papers on Louse Borne Relapsing Fever. I. Treatment of Louse Borne Relapsing Fever.** *J. Egyptian Pub. Health Ass.* 1946, Nov., v. 21, No. 8, 125–49. **II. Splenic Infarctions.** *Ibid.* 150–65, 3 charts. **III. Report on 139 Fatal Cases of Louse Borne Relapsing Fever.** *Ibid.* 166–82.

The author of these three papers is Director of the Fever Hospital, Imbaba, Egypt.

i. This paper records the study of 856 cases of louse-borne relapsing fever, 684 of which were treated with different arsenicals and 172 were kept as control.

The patients were divided into ten groups and each of nine groups was given a different treatment schedule with varying doses of NAB, Mapharsen, Mapharside and Glyvarsenyl: the tenth group served as a control.

Details are given of the results obtained in each group, in terms of fall of temperature, disappearance of spirochaetes, relapses and mortality: details of five fatal cases are given.

The final results of all the treatment schedules are shown in a table: the author does not, however, attempt to analyse them comparatively, and as several factors require to be taken into account, the table should be studied in the original.

ii. In 3,000 consecutive cases of louse-borne relapsing fever, infarction of the spleen was found in 75 (2·5 per cent.): there were 28 deaths. Most of the patients were between 20 and 65 years and males predominated. The condition is easily missed: it occurred mostly in the original attack and first apyrexial period.

In 52 cases the infarctions were simple: the remaining 23 were septic.

The signs and symptoms are discussed, and full details are given of four patients. Arsenical drugs were not found to be of use in treatment or in preventing occurrence of infarction: penicillin may prevent sepsis, if it is given early during the stage of simple infarction.

iii. Between January and July 1946, there were 7,379 cases of louse-borne relapsing fever admitted to Embaba Fever Hospital [this is printed earlier in the *Journal* as "Imbaba"]. Of these, 273 patients died. Autopsies were carried out on 139 of the fatal cases, and the results are discussed at length. It is noted that in 8 cases, foetuses of from 6 to 8 months were born prematurely, showing characteristic post-mortem signs of relapsing fever: all the mothers concerned had showed the specific spirochaete in their peripheral blood, and were actually suffering from relapsing fever at the time of miscarriage.

The morbid anatomy of relapsing fever, and of the complications found, is discussed and the records of 11 cases are given. *H. J. O'D. Burke-Gaffney*

HARTMANN, F. W. **Further Observations on Leptospirosis in Micronesia** *Science.* 1947, Sept. 26, 294.

This records information additional to that given by ALICATA [this *Bulletin*, 1947, v. 44, 665]. The investigation was carried out in this case on the island of Yap, in the Western Carolines, south and west of Guam.

In Yap Town, 28 rats were trapped alive; these comprised three species, *Rattus alexandrinus*, *R. norvegicus* and a third, provisionally identified as *R. exulans micronesiensis*. Pieces of kidney, removed immediately after each rat was killed by drowning, were preserved in 10 per cent. formalin for several months, and were then stained by a silver precipitation technique. No spirochaetes were found in any of the kidney sections.

The author concludes (although the number of specimens was small) that murine leptospirosis is not present in that area, possibly because Yap is geographically isolated. If, however, *L. icterohaemorrhagiae* was once introduced

into this area, where there is much rain and a large rat population, it might rapidly establish itself. *H. J. O'D. Burke-Gaffney*

SANTOS, M. A ocorrência da Leptospira icterohemorrhagiae nos ratos do Rio de Janeiro. [**Incidence of *Leptospira icterohaemorrhagiae* in Rats in Rio de Janeiro.**] *Rev. Brasileira Med.* Rio de Janeiro. 1947, June, v. 4, No. 6, 424–6, 2 figs. [12 refs.] English summary.

Between April 1944 and December 1946, the Plague Service of the Oswaldo Cruz Institute, under the direction of the author, examined 70,395 rats in Rio de Janeiro. Out of 1,467 guineapigs inoculated with material from these rats, 252 showed evidence of the specific leptospirosis.

The author refers to the literature, and notes the lack of correlation between *L. icterohaemorrhagiae* infection in rats and cases of Weil's disease in human beings: he recognizes that the latter "depend more on general hygienic conditions than on the presence of the germ." *H. J. O'D. Burke-Gaffney*

LEPROSY

AYCOCK, W. L. & GORDON, J. E. **Leprosy in Veterans of American Wars.** *Amer. J. Med. Sci.* 1947, Sept., v. 214, No. 3, 329–39, 5 charts. [36 refs.]

This paper is of special interest at a time when persons infected with leprosy during the war are being met with in Great Britain and other non-endemic areas. The authors refer to the well-known incidence of leprosy in the Southern United States, and describe the nearly complete disappearance of leprosy from Scandinavian immigrants, who settled in the cool climate of Minnesota under good hygienic conditions. This important fact makes it very unlikely that any appreciable number of new infections will arise from persons infected under war conditions and returning to Great Britain. The conditions under which infections usually arise are considered in accordance with present knowledge, and the importance of a study of infection among returning war veterans is pointed out.

In the case of the Spanish-American war, 32 war veterans were admitted to the U.S. Marine Hospital at Carville between 1921 and 1940, of whom 30 had served in leprosy endemic areas, mostly in the Philippines. The remaining two came from endemic areas of Louisiana and Texas. During the first World War period, 51 war veterans were admitted to the National Leprosarium, only 6 of whom had served in leprosy areas; but of 33 born in the United States all came from the Southern areas where foci of leprosy existed. In 1946, only one of 28 war veterans known to have leprosy had been born outside such infected areas. Both series of cases are tabulated and analysed to bring out the fact that whereas in the Spanish-American war most of the cases of leprosy originated in foci of the disease outside the U.S.A., in the two world wars the birthplace of the infected persons was largely in foci of leprosy, including those in the U.S.A. itself. Among 18 cases in the Spanish-American war from other than domestic foci of infection, exposure before the disease appeared ranged from 9 months to 32 years, but the actual dates of infection are unknown. In the first World War, all those infected were born in foci in the U.S.A. and developed the disease within a relatively few years, or already had the disease on enlistment. At present also 11 cases of the disease had existed in native-born subjects before entering military service; all but one had lived in home foci of infection and the remaining one had infected relatives. Their ages varied from 16 to

42 years against 32 to 66 in the Spanish-American war ; this also suggests that in the more recent wars infection occurred in foci in the U.S.A. where the infected persons had been born. Most of the patients from Louisiana have been of French origin. *L. Rogers*

CHAUSSINAND, R. Contribution à l'étude de la morphologie du bacille de Hansen. [**The Morphology of Hansen's Bacillus.**] *Ann. Inst. Pasteur.* 1947, July, v. 73, No. 7, 660–65.

In the course of his prolonged studies the author has distinguished four distinct morphological forms of leprosy bacilli, as follows : normal bacilli are rod shaped, sometimes with pointed ends ; they are of variable length and stain uniformly by Ziehl's method. Secondly, bacilli undergoing evolution are large, occasionally branched and with thickened ends and they do not always stain uniformly. They are found especially in macules and tuberculoid infiltrations and nerve cases which are showing resistance and tending to cure. They are not found in progressive lepromatous cases. They are also present in inoculated animals showing resistance to infection. Thirdly, bacilli undergoing division are divided into two or three nearly equal lengths by small unstained transverse intervals where they divide by fission ; they may show some granulation. They are never found in nerve cases not undergoing evolution and are less frequent in treated than in untreated cases ; but they are present in large numbers in globi in active cases of leprosy with rapid multiplication of the organisms. Fourthly, in degenerating lepra bacilli, disintegration takes place by progressive stages with the appearance of lightly staining granules in the rods, followed by gradual loss of staining power and the appearance of chains of granules, which in turn disintegrate to minute dots and then disappear. This last form increases *pari passu* with the clearing up of cutaneous cases under treatment. No proof has yet been furnished of the existence of an ultra-microscopic form.

[It may be of interest to recall that the reviewer, in 1917, recorded and illustrated increased granulation of lepra bacilli and their gradual disintegration and disappearance from nodules of the ears, with improvement under treatment by injections of soluble preparations of chaulmoogra oils (this *Bulletin*, 1918, v. 11, 407).] *L. Rogers*

CHAUSSINAND, R. A propos des essais de culture du bacille de la lèpre. [**Attempts at culturing Leprosy Bacilli.**] *Ann. Inst. Pasteur.* 1947, May, v. 73, No. 5, 433–8. [14 refs.]

This is a valuable summary of over 1,000 attempts to cultivate lepra bacilli in the course of ten years, with suggestive tests for the true organism to enable others to avoid the common fallacies of the hundred or so former workers who have incorrectly claimed success. SOULE and MACKINLEY appear to have come nearest, by obtaining minute colonies of the causative organism, but no one has obtained a series of subcultures. Readers should consult the original for a bibliography of former attempts and for a summary of the numerous culture media unsuccessfully employed by the present author. He concludes that workers have been misled through an apparent increase in the bacilli, with gradual dissolution of leprous tissue cells inoculated on media, and the carrying over of many of them on subculture. What may possibly have been a very slow appearance and increase of colonies of acid-fast bacilli with the characteristic appearance and arrangement of Hansen's bacillus may have been obtained occasionally, but subculture has proved difficult or impossible. The author advises the use of the following two tests to determine whether any apparent cultures are true leprosy bacilli or not. (1) The intradermal injection of

suspensions of Hansen's bacillus killed by heat gives negative local reactions after two weeks in lepromatous leprosy, and positive reactions in tuberculoid leprosy. On the other hand, similar injections of tubercle, paratubercle or Stéfansky's rat leprosy bacilli give more or less intense positive reactions in the case of all lepromatous persons who are sensible to tuberculin. (2) When Hansen's bacilli are injected into the general body cavity of the larva of the wax moth (*Galleria mellonella*) they are phagocyted by giant cells, but are digested very slowly so that they can be stained and easily recognized several days later in the insects. But tubercle bacilli and saphrophytic acid-fast paratuberculosis bacilli, formerly so frequently mistaken for Hansen's bacillus, are rapidly disintegrated and disappear from the giant cells within a few days. The use of these tests will enable the true character of any cultures obtained from the leprous tissues to be determined.

[The larva of the wax moth *Galleria mellonella*, is regarded as the "guineapig" of insect microbiology, and has been utilized in phagocytic studies of many bacterial species, owing to its varying capacity for phagocytic response to the inoculation of bacteria and other foreign particles. See also CAMERON, *J. Path. & Bact.*, 1934, v. 38, 441 and STEINHAUS, *Insect Microbiology*, 1946, 566, Comstock Publishing Co., New York.—Ed.] *L. Rogers*

CHAUSSINAND, M. Inoculation de la lèpre aux animaux. [**Animal Inoculation with Leprosy Material.**] *Ann. Inst. Pasteur.* 1947, July, v. 73, No. 7, 677–82.

The author summarizes in this paper ten years' experience of inoculations of animals with leprosy material. In the case of white mice, subcutaneous inoculation of material containing very numerous lepra bacilli produced only local lesions and alopecia; but three animals which survived intraperitoneal injections later showed scattered bacilli in the internal organs. Monkeys have also been inoculated by various routes. Intradermal and subcutaneous injections have produced local lesions only after three to five months; these disappeared again before long and left no trace nor was any multiplication of the bacilli found. Lepromatous nodules were implanted in the subcutaneous tissues, with the production of purulent lesions which healed slowly and were of an eliminative nature and not true infective lesions. However, the insertion of a leprous nodule into the peritoneal cavity did produce an infection, with the appearance of cutaneous lesions containing acid-fast bacilli; the tuberculin test was negative, but the Mitsuda was positive. Later the lesions resolved, with progressive disappearance of the Hansen-like bacilli from the tissues, and the Mitsuda reaction became negative. Inoculation of lepromatous emulsions into guineapigs by various routes gave no results, as the bacilli were eliminated more or less quickly. On the other hand, the insertion of a leprosy nodule under the skin of the nape of the neck produced a local infection.

The author concludes that the inoculation of animals with leprous material does not produce infections of a general nature, such as would afford opportunities for testing the value of therapeutic substances used in the treatment of the human disease. *L. Rogers*

OBERMAYER, M. E. **Diffuse Lepra.** *Ann. Western Med. & Surgery.* 1947, Aug., v. 1, No. 6, 225–31, 6 figs.

The author has had a large experience of this dangerous and easily overlooked form of lepromatous leprosy, since it accounts for as many as 60 to 70 per cent. of all lepromatous cases in parts of Mexico where he works, and 17 per cent. in other Mexican areas. As the disease develops slowly, with indefinite and not easily recognized symptoms, it easily escapes detection, yet is highly

infective. After discussing the differences between lepromatous and tuberculoid types of leprosy, the author describes the pure diffuse lepromatous form. Cutaneous nodules are absent and there is a diffuse infiltration of the skin of the whole body and a peculiar lepra reaction described by R. LUCIO as an *erythema necroticans*. Lucio called this form "spotted" or "Lazarine" lepra as early as 1851, and LATIPI studied it further in Mexico in 1937. The unique lepra reactions appear three or four years after the onset of this type of the disease as tender and painful erythematous and slightly infiltrated small macules on the extremities and face, which develop central necrosis leaving superficial, sharply circumscribed atrophic scars; these lesions are illustrated by five photographs. Osseous destruction may result in a saddle nose, but the eyes are not affected. The eyelashes and eyebrows are frequently lost and alopecia of the scalp may follow. Progressive weakness ensues with death, occurring after an average of eight years; the Mitsuda reaction remains negative throughout, indicating absence of resisting power. Numerous lepra bacilli are found in the diffusely infiltrated skin in all parts of the body; unfavourable reactions follow the use of chaulmoograte or iodides.

L. Rogers

TISSEUIL, J. Deux types de lèpre cutanée tertiaire, dermique rouge en nappe, hypodermique blanche en nodule. [**Two Types of Cutaneous Tertiary Leprosy.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 5/6, 147–9.

The author describes red and white tertiary cutaneous leprotic lesions which he thinks are liable to be confused. The red form occurs particularly on the body in the form of extensive, isolated thickenings or nodules of a yellow or red colour showing necrosis and very numerous lepra bacilli on section, and it may cicatrize to leave white radiating scars; it tends to develop rapidly.

On the other hand, the white lesions are more frequent on the face and extremities in the form of isolated nodules up to the size of an almond; these are situated in the subcutaneous tissue and freely movable under the dermis, which is pale white. They contain numerous polynuclear cells and lepra bacilli and tend to soften and discharge through the skin, leaving ulcers which heal slowly. They are easily excised and have a fibrous coating; they discharge many bacilli and have a longer duration than the red form. *L. Rogers*

MONTESTRUC, E. & CAUBET, P. **Ainhum in a Leper.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Oct., v. 41, No. 2, 187–8, 2 figs.

A lesion of the little finger illustrated by a radiograph and a photograph.

CUTTLE, T. D. **Failure of Streptomycin in the Treatment of Leprosy.** *Amer. J. Med. Sci.* 1947, Oct., v. 214, No. 4, 385–8, 2 figs.

Report of a case.

HELMINTHIASIS

ELSDON-DEW, R. **Zinc Sulphate Flotation of Faeces.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Oct., v. 41, No. 2, 213–16, 1 fig.

The zinc sulphate flotation technique of FAUST *et al.* [this *Bulletin*, 1939, v. 36, 144: *ibid.* 1940, v. 37, 62] is coming into increasingly prominent use for the concentration of ova and cysts in faeces: it has, however, the disadvantage that trophozoites of protozoa are destroyed by the repeated centrifugation.

The author, in Durban, compared this technique with the direct faecal film in the examination of 1,539 routine specimens of stools, derived mostly from cases of suspected amoebiasis. For the reason noted above, findings for protozoa refer to cystic forms only.

The results are clearly set out in the form of two tables and a chart: one of the former shows the exact findings of six species of protozoa and six species of helminths, by the direct and flotation methods, separately and together: conflicting results with the double techniques are also shown, together with the totals of all positive findings. The second table indicates the relative efficiencies of each method, singly and together, and includes a column showing the ratio of positive results by the zinc method to that of the direct, expressed as percentages. The chart compares graphically the proportion of positive findings, in the form of appropriately shaded circles.

Four hundred and twenty (36·6 per cent.) specimens were negative by both methods: in the remainder, there was considerable variation in the total of positive findings, from 6 and 11 in the case of *Chilomastix mesnili* and *Schistosoma mansoni* to some 200 in the case of *E. histolytica* and *E. coli* and hookworms, and some 600 in the case of *Ascaris* and *Trichuris*.

For a statistical appraisal of the results, the tables should be consulted: but it may be said that, on the whole, there was a striking gain in positives for nearly every species of parasite when the zinc sulphate flotation was used. Protozoal cysts floated well, especially those of *Iodamoeba bütschlii*: the absence of faecal débris made ova and cysts easy to find.

Nevertheless, some ova did not usually float well, especially those of *Taenia* and *Schistosoma mansoni*: they were often found in the final centrifuged deposit.

The author calculates that the average overall gain obtained by the use of Faust's zinc sulphate flotation amounted to 179 per cent.: in the case of hookworm, *Giardia* and *Iodamoeba bütschlii*, it was over 500 per cent. The technique is a very valuable diagnostic aid in the examination for intestinal parasites: but the author believes that the direct film still remains the method of choice, since trophozoites may also be detected with its use. Where possible, both techniques should be employed. *H. J. O'D. Burke-Gaffney*

DE MEILLON, B. **Aspects of the Natural History of Bilharzia in South Africa.** Read at a Medical Congress, East London, South Africa, 1947. 6 pp. [17 refs.].

This paper, read at a medical congress in East London, South Africa, is an able summary of the position as regards human schistosomiasis in the Union. *Schistosoma haematobium* is found throughout the whole Transvaal north of about 26°S., and there is a strip of country, also infested, down the coast as far as Port Elizabeth. Snails capable of acting as intermediate hosts exist in areas hitherto unaffected by the disease, but the increase which is taking place in the movements of labourers may bring infection to new areas. *Schistosoma mansoni* was hardly known in the Union in 1934, but since then indigenous cases have been found in Natal, N.E. Transvaal, Central Transvaal, Eastern Transvaal, and Swaziland. This infection is apparently spreading actively, having been introduced from the north.

The author remarks on the difficulties experienced in the identification of molluscs, and on the scarcity of experts on the subject. In the Union, the following molluscan hosts have been found: for *S. haematobium*:—*Physopsis africana, Physopsis globosa, Bulinus tropicus, Bulinus forskali* and (doubtful) *Lymnaea natalensis*. The host of *S. mansoni* is *Planorbis* (*Biomphalaria*)

pfeifferi. The author gives a list of places where these snails are found; they are much more widely distributed than the corresponding schistosomes.

The ecology of these snails has not been studied systematically, and there is a need for research on this subject. It is, however, known that snail-spawn is deposited on aquatic plants, and may be transported considerable distances on the legs of wading birds; it is also known that some snails prefer mud rich in organic matter such as faeces. There is a general impression that rivers running west in the Union are not dangerous in respect of schistosomiasis, and this is largely true, because the rivers are in their natural state, perennial, with sandy bottoms and subject to violent flushing so that there is little true aquatic vegetation; snails do not flourish in such streams. If these rivers are dammed, however, they will become suitable for the snails.

The author gives a detailed description of the laboratory techniques for identification of cercariae from wild-caught snails, for infection of laboratory snails, and for their maintenance. These details must be sought in the original.

The paper ends with a warning that the great industrial development planned for the Transvaal, which will involve a large increase in population and which has already led to the impounding of water in the Vaal river, may mean a very great spread of schistosomiasis if the relevant snails become established; the prospect, if this happens, will be grim. The author also notes that African immigrants from tropical areas are not permitted to settle in urban areas, and that they therefore seek the small farms close to towns, and may infect the snails in the waters about those farms. *Charles Wilcocks*

i. BASSÈRES, M. S. & PANTOJA, W. P. Esquistossomose.—Prevalência de *S. mansoni* na população humana. [**The Prevalence of** *Schistosoma mansoni* **in Man in Part of Minas Gerais, Brazil.**] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1947, v. 1, No. 1, 135–48, 1 fig. & 1 map. English summary.

ii. —— & ——. Esquistossomose. Prevalência de *S. mansoni* em Planorbídeos. [**The Prevalence of** *Schistosoma mansoni* **in Planorbid Snails in Part of Minas Gerais, Brazil.**] *Ibid.*, 149–62. [12 refs.] English summary.

i. The authors examined faeces from 5,314 persons (about 15 per cent. of the population) along the Victoria-Minas railway. The specimens were examined by the Stoll-Hausheer technique. Part of the route lies along the Rio Doce, and three zones were recognized. The first lay away from the river, and here the proportion of persons infected with *S. mansoni* was 0·9 per cent. The second zone lay entirely along the river, with an index of infection of 21·1 per cent. The third zone lay partly along the river, and partly away from it, where the railway diverges from the main stream, and in this zone the index of infection was 12·9 per cent. Incidence reached its peak in the age group 15–24, and was rather greater in males than in females at all ages.

The infection rates in planorbid snails (see below) varied from nil to 11.1 per cent. Details of the findings are set out in a series of tables.

ii. In connexion with the investigations in man referred to in the preceding abstract, the authors examined 5,248 planorbid snails taken in the three zones. Most of the snails were *Australorbis olivaceus*, a well-known intermediate host of *S. mansoni*, but other genera were also examined, in small numbers.

In Zone I, where human infection is light, no infected snails were found. In Zone II, infection with *S. mansoni* was found in 11·1 per cent. of 4,297 snails; and in Zone III in only 1·4 per cent. of 517 specimens. The snails were found chiefly in creeks, springs and ditches, and there was evidence that they may

spread from the main streams of the Rio Doce, up the tributaries. The basin of the Rio Doce apparently constitutes a single unit in relation to schistosomiasis. *Charles Wilcocks*

i. MALDONADO, J. F. & ACOSTA MATIENZO, Josefina. **The Development of** *Schistosoma mansoni* **in the Snail Intermediate Host,** *Australorbis glabratus. Puerto Rico J. Pub. Health & Trop. Med.* 1947, June, v. 22, No. 4, 331–73, 29 figs. [Refs. in footnotes.] [Spanish version 374–404.]

ii. —— & ——. **Larval Cycle of** *Schistosoma mansoni* **in its Snail Intermediate Host,** *Australorbis glabratus. Kuba.* Habana. 1947, Mar., v. 3, No. 3, 69–72, 5 figs.

i. "1. The miracidium of *S. mansoni* bears a close resemblance to that of *S. haematobium*. In addition to other structures described in previous accounts, it is also provided with an anterior *terebratorium* and pairs of antero-lateral and postero-lateral papillae. What has been described by others as clusters of lateral secretory glands, with their corresponding ducts, is believed to be ganglionic nerve cells and nerve tracts that run to the antero-lateral papillae. A germinal epithelium has not been observed.

"2. The miracidium penetrates into the molluscan host by actual perforation of the epiderm of the head-foot organ, the tentacles, or the mantle collar. On rare occasions, a larva may gain access to the shell cavity and from there penetrate and settle in rather distant locations.

"3. The snail may be simultaneously parasitized by numerous miracidia. However, during the first days of infection, many will fail to develop, so that the number of mother sporocysts in multiple infections is smaller than the number of miracidia that actually penetrate.

"4. Implantation and subsequent development occurs close to the point of entrance. Within five hours the miracidium loses its motility and sheds its ciliary membrane. By the twenty-fourth hour the germ cells in the larva begin to divide. The parasite may then be called a mother sporocyst.

"5. By the forty-eighth, many of the mother sporocysts may appear as fairly elongated, simple, thin-walled sacs full of germ cells. The body begins to develop transverse constrictions that make the parasite appear like a series of separate chambers. Beyond the second day, and up to the twentieth, the sporocyst grows markedly in length, becoming an intricate organism with numerous constrictions and convolutions. Essentially, however, it is a long, thin-walled tube. There is no evidence of motility in the mother sporocyst *per se*. Migration of this stage through the snail tissues is, therefore, highly improbable.

"6. Whenever the mother sporocyst develops close to the surface of the head-foot organ, in the tentacles, or in the mantle collar of the snail, a permanent tumefaction arises. The swelling becomes perceptible on the fourth day of infection and grows in size with advancing age.

"7. The daughter sporocysts can be first observed within the mother form by the fourth day of infection, appearing as undifferentiated masses of cells. By the eighth day, many are already elongated and motile, and by the eighteenth, they begin to migrate towards the distal glandular tissues of the snail where they finally settle and grow. In heavy infections some daughter sporocysts may fail to reach such sites, developing in other parts of the host. A mother sporocyst may give rise to hundreds of daughter forms.

"8. Cercariae arise within the daughter sporocysts by germ ball formation. The first cercarial germ balls may appear while the sporocyst is still on its migratory phase. Once in its final habitat, numerous other balls are produced.

Each one of them elongates after reaching a certain size and develops a constriction at the middle whereby the tail arises. Subsequently, the other organ systems are formed and, in a few days (*ca.* one week), the mature cercaria is ready to emerge from the snail."

ii. This is a shorter version of the above.

OTTOLINA, C. **The Rectoscopic Biopsy by Transparency. A New Diagnostic Method for** *Schistosoma mansoni*. *Amer. J. Trop. Med.* 1947, Sept., v. 27, No. 5, 603–6.

The author discusses the origin and rationale of the rectoscopic biopsy for the diagnosis of *Schistosoma mansoni* infections described by himself and ATENCIO in 1943 [this *Bulletin*, 1944, v. 41, 945].

In the test, a fragment of mucous and submucous tissue from the upper half of the rectal ampulla is taken from the middle Houston valve about 10 cm. from the anus in the area drained by the superior haemorrhoidal veins: this tissue is digested for 3 to 4 hours in 4 per cent. caustic potash solution at 60° to 80°C., and examined microscopically after centrifugation.

The author discusses his experience and that of others with the use of this technique, and refers especially to the work of RINCON URDANETA (*Rev. Policlinica Caracas*, 1945, v. 14, 325). The value of the rectoscopic method compared with stool and intradermal tests is emphasized and comparative figures from the literature are given. The rectoscopic biopsy is a direct method with only a negative error and this has an advantage over indirect methods: nevertheless its value would be greater if these false negatives could be avoided.

One factor which seems to influence these errors is that caustic potash digestion, although it made it easier to find eggs in light infections, involved further and harmful manipulation.

Direct microscopic examination of the fragments before digestion did not prove adequate: many devices were tried to make the tissue fragments transparent and eventually it was found that this could be achieved by immersing them for 3 to 5 minutes in fresh water. This dissolves the haemoglobin and the eggs appear in characteristic strings: also the living fragment absorbs water quickly and after 3 to 5 minutes becomes a watery globule: this is then compressed between two slides, a drop of water is added, the whole is covered and pressed gently and a thin transparent film can be seen. The eggs can be easily seen in the film by focussing with the lower power of the microscope at different levels.

The method is simple and rapid and, in light infections, avoids losses which may occur during caustic potash digestion. An important advantage is that normal eggs containing living miracidia are often seen by the transparency method in specimens from untreated patients: such miracidia are killed by the digestion method. This is of therapeutic significance, as it aids in determining the course and results of treatment.

It is stated that the movement of miracidia in individual eggs can be detected with a high power without difficulty: and it is even possible to puncture an egg with a fine needle "to deliver the miracidium under microscopic control".

The author concludes by recording that rectoscopic biopsy by transparency presents a clinical diagnosis of *S. mansoni* in a few minutes: "the high figures already obtained with the rectoscopic biopsy alone suggest a thorough revision of our clinical knowledge of schistosomiasis" [see also this *Bulletin*, 1947, v. 44, 330]. *H. J. O'D. Burke-Gaffney*

DA SILVA, J. R. & COSTA, N. A biópsia retal no diagnóstico e no contrôle da eficiênca terapêutica da esquistosomiase de Manson. [**Rectal Biopsy in the Diagnosis and Therapeutic Control of** *Schistosoma mansoni* **Infections.**] *Hospital.* Rio de Janeiro. 1947, Aug., v. 32, No. 2, 219–33, 7 figs. [19 refs.] English summary.

The authors found *S. mansoni* eggs in 13 of 100 patients sent for diagnosis of schistosomiasis by the rectal biopsy technique : in only 4 of these 13 patients were faecal examinations positive after repeated search. On the other hand, in one patient faecal examination was positive and two biopsies were negative.

The authors refer to the previous work of HERNÁNDEZ MORALES and MALDONADO [this *Bulletin*, 1947, v. 44, 330] and discuss their observations on the possibility of estimating therapeutic efficacy by the morphological study of schistosome ova found in biopsy material.

They conclude that rectal biopsy greatly simplifies the diagnosis of *S. mansoni* infections, especially where laboratory facilities are limited ; it is simple, quick, without risk and does not require the detention of the patient in hospital. The paper is illustrated with seven photomicrographs showing ova that were detected. [See OTTOLINA, above.] *H. J. O'D. Burke-Gaffney*

WRIGHT, W. H., MCMULLEN, D. B., BENNETT, H. J., BAUMAN, P. M. & INGALLS, J. W., Jr. **The Epidemiology of Schistosomiasis Japonica in the Philippine Islands and Japan. III. Surveys of Endemic Areas of Schistosomiasis, Japonica in Japan.** *Amer. J. Trop. Med.* 1947, July, v. 27, No. 4, 417–47, 7 figs.

The authors explain that their report lacks the usual historical review since for various reasons, they had not full access to the Japanese literature on the subject. On the other hand, the information collected on the spot from doctors and health workers has been incorporated, and in spite of the language difficulties which were encountered, supplies data not otherwise available in published accounts of schistosomiasis in Japan. The Commission surveyed five known endemic areas of schistosomiasis, with a view to delineating the extent of these areas and gaining information which would assist in the protection of troops stationed in them. "On entering an endemic area, as much information as possible concerning the status of the disease was obtained from prefectural and local health authorities and from practicing physicians. Based on this information, certain schools in various parts of the area were selected, and a representative number of stool samples obtained from children in the higher age groups (8 to 15 years) for microscopic examination for schistosome eggs. Surveys were then conducted in various parts of the area for *Oncomelania* (*Katayama*) *nosophora*, the snail intermediate host of *Schistosoma japonicum*. When the snails were found, sufficient numbers were collected for transport to the laboratory for examination for incidence of infection.

"All stool examinations conducted by the commission were carried out with the use of the plain sedimentation technique. This technique had previously been found to be the most efficient one for practical use in the field, through research carried out by members of the commission on Leyte and other islands. The technique consisted in taking five grams of feces, stirring the sample in water, straining the material through four layers of surgical gauze into a 250 cc. conical urinalysis flask, allowing the material to sediment, and pouring off the supernatant fluid. At least three decantations were made. One drop of the final sediment was placed on a slide and examined under the microscope. In the examination of school children in Japan, the commission followed the practice of examining two 22×22 mm. cover glass preparations or one 22×40 mm. cover glass preparation from each sample." A total of 1,688 school

children were examined by the Commission in the five endemic areas; of these, 381 (22·6 per cent.) were infected with *S. japonicum*. A higher proportion of males than females were found to be infected, 29·2 per cent. of the boys as compared with 16·7 per cent. of girls. This finding is in agreement with that of the Japanese who found a preponderance of infection in all cases amongst the male population and ascribed it to "their greater opportunities of acquiring infection".

The following summaries of the Commission's surveys show that the incidence of infection in the human population and in the snail vector varied considerably in the five areas.

(1) *Tone River Area, Chiba and Ibaraki Prefectures.*—This has the lowest infection rate of any area in Japan, and only 3 out of 390 school children, examined in six localities, were found to be infected. The Commission was unable to find specimens of *Oncomelania* (*Katayama*) *nosophora*, the most important snail vector, although this species of mollusc undoubtedly occurs in some parts of the area.

(2) *The Kofu Area in the Yamanashi Prefecture.*—In contrast to the Tone River area, this is the most important schistosomiasis district in Japan, and in spite of the intensive control which has been carried on since 1942, the commission found that 245 out of 458 (53·5 per cent.) school children were infected. This figure is more than double that previously recorded in the same school by doctors of the Japanese Health Department, who had estimated that 24·2 per cent. of the children were infected. The same Japanese Health Authorities had also examined the general population with the following results:—

Results of stool examinations for schistosomiasis carried out in the Kofu area by health authorities of Yamanashi Prefecture between May 1, 1944 and April 30, 1945.

Area	No. Persons Examined	No. Persons Positive	Per cent Positive.
Control	81,031	5,026	6·2
Under control	57,013	2,983	5·2
Uncontrolled	22,862	2,588	11·3
Totals	160,906	10,597	6·6

That these figures are well below the true infection rate is suggested by the American Commission's comment that "all these examinations were made by means of a single fecal smear with what the commission regarded as inadequate equipment". The evidence obtained from the same source indicates that certain domestic and wild animals are responsible for the transmission of infection to the snail intermediate host.

The snail vector, *O. nosophora*, was found without difficulty in the Kofu Area, and of 200 snails which were crushed and examined, three were found to be infected.

(3) *The Namazu Area in the Shizuoka Prefectures.*—Previous data concerning the infection in the general population between 1920 and 1926 were published in 1933, and showed that about 4 per cent. of the total population were infected. Since that date, the Japanese have drained a large swamp in the centre of the area, and this measure has probably materially reduced the schistosomiasis rate. In the present survey, the American Commission found 14 out of 155 (9 per cent.) of the children infected with *S. japonicum*. The snail vector was localized to one area, where, out of 315 *O. nosophora* examined, 2 (0·63 per cent.) were infected.

Results of examinations for S. japonicum *infection in lower animals in the Kofu area carried out by health authorities of Yamanashi Prefecture between May 1, 1944 and April 30, 1945*

Species	No. Examined	No. Positive	Per cent. Positive
Cattle	7,059	2,184	30·9
Goats	1,118	158	14·1
Dogs	353	176	49·9
Horses	967	0	0
" Rats " (probably including field mice, *Microtus* spp.)	1,707	656	38·4
Moles	68	13	19·1
Mustela sp.*	10	9	90·0

*Probably *Mustela* (*lutreola*) *itatsi*.

(4) *The Fukuyama Area in the Hiroshima and Okayama Prefectures.*—Through the organized control work which has been carried on in this area over the past 30 years, the disease has been greatly reduced and the distribution of the snail intermediate host considerably restricted. The disease is now confined to the fringes and to the centre of the area, and of 357 children examined from these areas, the Commission found 34 (9·5 per cent.) to be infected. Control measures by the Japanese had considerably reduced the numbers of *O. nosophora*, which was now confined to an area of approximately four square miles. Out of 501 snails collected from this area, 19 were found infected, the percentage of infection in the snails collected from different localities varying from 0·5 to 15·8 per cent.

(5) *Kurume Area in the Saga and Fukuoka Prefectures of Kyushu.*—Considerable published Japanese data concerning the previous incidence of schistosomiasis in this area were available to the Commission, but the differences in the techniques employed and in numbers examined made it difficult to compare the results. The Japanese figures depict a steady diminution in the incidence of the disease, but the present authors' examination of 328 children from three schools revealed an infection rate of 25·9 per cent., a figure which suggests that there has been little, if any, decrease in the schistosomiasis infection rate in this area during the past 20 years. The distribution of the snail intermediate host varied considerably, *O. nosophora* being found in abundance in the areas with a high human incidence of infection, and being absent from, or scanty in, areas with a low human incidence of schistosomiasis. The infection rate among the 510 snails which were dissected varied from 4 to 9·5 per cent. according to the area from which they were collected.

This paper contains references to other helminth infections which were observed in the specimens of faeces examined for the presence of *S. japonicum* ova. *R. M. Gordon*

VOGEL, H. & MINNING, W. Ueber die Einwirkung von Brechweinstein, Fuadin und Emetin auf Bilharzia japonica und deren Eier im Kaninchenversuch. [**The Action in Guineapigs of Tartar Emetic, Fouadin and Emetine on** *Schistosoma japonicum* **and its Eggs.**] *Acta Tropica.* Basle. 1947, v. 4, Nos. 1 & 2, 21–56; 97–116, 9 figs. [22 refs.] English summary.

Experiments were carried out on rabbits to ascertain the nature of the effects of certain drugs on the adult *S. japonicum* and whether they would destroy eggs in the tissue of the host.

The animals were exposed to infection with a known number of cercariae, and after the commencement of egg passage 29 of the rabbits were treated with tartar emetic, 7 with fouadin, 10 with emetine and 6 were kept as untreated controls. The dosage was 2·5 mgm. (intravenously) for tartar emetic, 0·11 cc. (intramuscularly) for fouadin and 2 mgm. (intravenously) for emetine. The dosage and intervals between doses was kept constant throughout, but the number of injections varied from 3 to 24.

Tartar emetic.—At least 9 to 12 injections were required to cause the eggs to fail to hatch. It was concluded that after 6 injections, about half the adult worms still survived; about one-fifth survived after 12 injections and only about one-tenth after 18 injections. The males were more resistant than the females. Five of 12 animals which had received 15–18 injections, and one of seven animals with 12 injections, were completely cured.

The treatment produced a variety of changes in the adult worms; a marked diminution in size which was proportional to the number of injections; the contents of the intestines were reduced and altered; the testes, ovary and yolk glands were reduced in size and later almost completely destroyed; egg formation was interrupted and then ceased; but one to three months after treatment, the worms which survived recovered their normal appearance and functions.

Fouadin.—The effects of this drug on the worms were, in the main, similar to those produced by tartar emetic, but to a lesser degree.

Emetine.—With this drug, viable eggs temporarily disappeared from the faeces of some of the treated animals. The worms did not decrease in number nor in size and the genital organs were unchanged; but the yolk glands reacted by secreting a mass of yolk cells which entered the ovary and caused a club-shaped swelling of the uterus, interfering with the functions of these organs. Some of the females were unaffected and continued to lay normal eggs. None of the ten animals was cured. *J. J. C. Buckley*

González Castro, J. Fasciolosis hepatica en general, y en especial en España. [**Infestation by** *Fasciola hepatica*, **in particular as it occurs in Spain.**] *Med. Colonial.* Madrid. 1947, Oct. 1, v. 10, No. 4, 221–68, 2 figs. & 3 pls. [Numerous refs.]

The first part of this article need only be mentioned, as the facts related are well known to readers of this *Bulletin*. It deals with a description of *F. hepatica*, its life-history, epidemiology, geographical distribution, intermediate hosts, pathology of infection, treatment and prophylaxis.

The second part, relating to its incidence in Spain, is of more interest and importance from our point of view. It was first reported in sheep by Martín de la Calle in 1890 and in the same year in a workman in Segovia. García Sola's report of a case in 1884 is stated by López-Neyra (in 1933) to have been erroneous, the ova of *Diphyllobothrium* being mistaken for those of *Fasciola hepatica*. Cases are evidently rare. The author mentions one in 1944 in a woman of Almuñécar (the ova were found in the faeces and in the bile); five suspected cases in 1945, of which one was confirmed, another had eosinophilia but no ova were seen in the stools and the use of a duodenal sound was not practicable. In 1946, a third case was proved, a sister of the first in Almuñécar, and soon after one was reported to the author by a doctor who had seen an ovum of *F. hepatica* in the stool of a child suffering from an obstinate diarrhoea. There were evidently others, for the author states that "in 3 years six cases have been seen in Spain." Probably—one might say, certainly—with more thorough examination and more doctors on the look out for cases, the numbers positive would rise, but they cannot as yet be numerous.

There is need to find out more regarding infestation of sheep, cattle and goats; *Limnaea truncatula* is far from uncommon in Barcelona and elsewhere.

H. Harold Scott

VON BONSDORFF, B. **In which Part of the Intestinal Canal is the Fish Tapeworm found? A Questionnaire.** *Diphyllobothrium latum* **and Pernicious Anaemia IX.** *Acta Med. Scandinavica.* 1947, Nov. 5, v. 129, No. 2, 142–55.

This paper continues the author's work on pernicious tapeworm anaemia [this *Bulletin*, 1947, v. 44, 1081; 1948, v. 45, 97].

Portions of the tapeworm *Diphyllobothrium latum* may be vomited by carriers or expelled with the faeces; whether these episodes are accidental or whether they are indications that the worm can exist more permanently in the upper or lower parts of the alimentary canal is uncertain.

To answer the question put in his title, the author sent a questionary to 700 medical practitioners and specialists throughout Finland, especially to those in the areas most heavily infested with tapeworm. The questions asked for information regarding possible evidence of tapeworms in vomited material, at abdominal operations, autopsies and X-ray examinations, and in unusual situations.

The fact that only some 60 replies were received seemed to be an indication that many doctors had no clear conception of the implication of the question or, in some cases, that definite facts were not available. Nevertheless, the answers received were informative and, for the most part, were in agreement: and the paper consists of a detailed examination and analysis of the replies. These contain much information and should be studied in the original.

The fact, incidence, cause and diagnostic difficulties of tapeworm vomiting are discussed: among the 100 cases of this condition which comprised the material, a strikingly large number showed an anaemia which was either definitely, or at times, probably of a pernicious character: this represented a higher incidence of pernicious anaemia than would be expected among tapeworm-carriers generally. The author concludes that tapeworm vomiting as a diagnostic characteristic has been largely overlooked: the attack may be very sudden, and associated with collapse, severe pain and a sense of suffocation, and, in its early stages, may be confused with the more usual acute surgical abdominal conditions. The vomited worm may be several metres long. The author believes that in many cases the vomiting may possibly be assumed to indicate that the worm is found in the upper part of the small intestine.

Replies received from surgeons indicated unanimously that the fish tapeworm was found most generally in the ileum, rarely in the jejunum and sometimes in the colon: in the last situation, there is doubt whether it may not have been there by chance. It is therefore uncertain whether the worm is in fact in the habit of living in the colon.

Reports of post-mortems seem to confirm these findings, but the material available was incomplete and it could not be decided from it with any certainty whether the localization of the worm differed in anaemic and non-anaemic characters.

Roentgenological findings were consistently negative. Few unusual localizations were reported: these included the finding, at operation, of a gall-bladder full of tapeworm and of the worm giving rise to intestinal obstruction.

So far as the available material goes, the evidence seems to favour the belief that *D. latum* is found most frequently in the upper small intestine, particularly in the ileum, and that anaemia among carriers has been seen more frequently in the case of those who had vomited the worm.

[The paper contains a considerable amount of information regarding the different conditions reported and their incidence.]

H. J. O'D. Burke-Gaffney

CLAPHAM, Phyllis A. **On the Occurrence of** *Davainea madagascariensis* **on the African Mainland.** *J. Helminthology.* 1947, v. 22, No. 1, 47–8.

Identification of a specimen from the stool of a patient in South East Africa.

McGILL, R. G. **Cysticercosis resembling a Myopathy.** *Indian J. Med. Sci.* 1947, Sept., v. 1, No. 3, 109–14. [10 refs.]

Report of two cases.

BISHR, M. S. **A Case of Pulmonary Hydatid Cyst with Asthma.** *J. Roy. Egyptian Med. Ass.* 1947, July, v. 30, No. 7, 341–6, 4 figs.

JENKINS, T. W. **Hookworm Survey.** *Med. Bull.* New Jersey. 1947, Oct., v. 7, No. 2, 113–18.

The author, who is a medical officer of a Company in Port Moresby, examined specimens of faeces from 232 natives of Papua. Flotation and direct methods were employed: the former consisted of emulsifying the faeces in 3 per cent. caustic soda, and adding saturated sugar solution: for the direct method, the specimen was emulsified in the caustic soda solution only. In the flotation method, preparations were made by transferring material from the surface of the sugar emulsion to a slide, by means of the applicator stick which had been used to mix the faeces. The direct method was found satisfactory, and it was only necessary to add the sugar solution for flotation purposes when direct smears were negative.

A total of 188 (81·06 per cent.) specimens were found to contain hookworm ova. Of these, 96 were classed as moderate to heavy infestations and 92 as light.

In 40 (17·24 per cent.) cases, ova of *Trichuris trichiura* were found: hookworm ova were present in 38 of these. No other helminth ova were detected: it was, however, noteworthy that live *Sarcoptes scabiei* was found in 27 (11·64 per cent.) specimens; this is attributed to contamination of the tins at the time of passing of the specimens.

The persons found infested were treated with 3 cc. of tetrachlorethylene, on the morning after an evening dose of 1 oz. of magnesium sulphate had been given: a second dose of salts was given after the anthelminthic. It is stated that "untoward reactions were noted in a small number of cases so treated". These took the form of somnolence, giddiness and—in one or two cases—incoordination, thickness of speech and a general appearance of intoxication. All toxic manifestation disappeared within an hour or two. Checking of results by repeated faecal examination was undertaken in a "few cases" only: these latter were free from ova.

The author recommends that new recruits should be treated on joining the Company and at intervals of 6 months, in view of the prevalence of hookworm infestation "among Papuan natives recruited from all parts of the Territory".

H. J. O'D. Burke-Gaffney

ZELIGS, M. **Intradermal Tests with** *Dirofilaria immitis* **Extract in Human Filariasis.** *U.S. Nav. Med. Bull.* 1947, Sept.–Oct., v. 47, No. 5, 824–6.

Large numbers of troops in the Pacific area, especially in Samoa and Wallis, were exposed to filariasis, and many of them contracted it: since *Mf. bancrofti* is rarely demonstrable in the blood of returned servicemen and the clinical

differential diagnosis may be perplexing, the author and his colleagues applied the intradermal test with *Dirofilaria immitis* antigen to men who had served in the Pacific.

He discusses the varying results of this test obtained by TALIAFERRO *et al.* [this *Bulletin*, 1931, v. 28, 214] and SAUNDERS *et al.* [*ibid.*, 1947, v. 44, 108].

In the present case, 200 men were tested at the U.S. Naval Hospital, Aiea, Oahu, between July 1944 and August 1945. A saline extract of *D. immitis* was used, standardized to contain 0·0005 mgm. of protein per cc. The test was made intracutaneously in the forearm with 0·1 cc. of the solution. No control antigen was used. The results were recorded as Immediate (after 15 minutes and 1 hour) and Delayed (after 24 hours) in terms of 1 plus to 4 plus, according as there was, in the former, erythema of from 1 to 4 cm., from that with no weal, up to a weal with pseudopods: and, in the latter, erythema between 1 and 4 cm., with increasing degrees of subcutaneous oedema.

Results of 2 plus or more were called positive. Of 126 patients with a diagnosis of filariasis, 94 (75 per cent.) were positive: of 21 who had lived in Samoa, but who had no evidence of filariasis, 6 (29 per cent.) were positive. In the case of 53 patients who had not been in Samoa or Wallis (and therefore presumably had not been exposed), 10 or 19 per cent. were positive.

In the filariasis group, of 64 immediate reactors, 13 were negative at the end of 15 minutes, but positive at the end of an hour: 9 of these were also negative after 24 hours, so they would have been missed if no reading had been taken at 1 hour.

The author notes that SAUNDERS *et al.* (*loc. cit.*) had found 81 per cent. of positive reactors among filariasis patients who had been in Samoa, but only 45 per cent. in those who had not. The present series revealed no such difference; but among those not diagnosed as having filariasis, the author found 29 per cent. of positives among those exposed in Samoa, compared with 19 per cent. in those who had not been exposed there. Three positive reactors were found among five patients having *Schistosoma japonicum* infections: no positive results were found in four persons suffering from hookworm or in one each suffering from *Ascaris*, *Strongyloides* and *E. histolytica*.

The author concludes that, while the intradermal test with *D. immitis* antigen is of some diagnostic value for filariasis, it cannot be depended on exclusively, as it was negative in 25 per cent. of suspected cases and positive in 19 per cent. of controls. *H. J. O'D. Burke-Gaffney*

AGAVRILOAE, A. Consideraţiuni asupra unui caz de Filaria bancrofti. [**A Case of *Wuchereria bancrofti* Infection (in Rumania).**] *Rev. Ştiinţelor Med.* Bucharest. 1946, Sept.–Dec., v. 36, Nos. 9/12, 719–27. French summary (3 lines).

This paper describes the finding of *Mf. bancrofti* in a Russian airman in Rumania: it is stated to be the first case reported in that country.

H. J. O'D. Burke-Gaffney

HARTZ, P. H., HUGENHOLTZ, M. J. & VAN DER SAR, A. **Helminthic Infection of the Wall of the Gallbladder.** *Arch. Pathology.* 1947, Apr., v. 43, No. 4, 408–11, 2 figs. [Refs. in footnotes.]

In the wall of the gall bladder, removed from a woman aged 28, a native of Surinam, the authors found a necrotic worm in a subserous lymphatic vessel, and eosinophil infiltration. The patient had, some years earlier, shown microfilariae in the blood, but schistosomiasis had never been diagnosed. The

worm could not definitely be identified, but it was too large for a larval *Ascaris*, and was probably not a schistosome. The authors think that it was probably a filaria [presumably *Wuchereria*]. *Charles Wilcocks*

BLOEM, T. F., HUYSINGA, J. K. & WILDERINK, G. C. [**Treatment of Oxyuriasis with Phenothiazine.**] *Nederl. Tijdschr. v. Geneesk.* 1947, July 19, v. 91, p. 1946. [Summary taken from *J. Amer. Med. Ass.* 1947, Nov. 8, v. 135, No. 10, 676.]

Bloem and his associates regard phenothiazine as an excellent remedy against oxyuriasis. The patient must be kept under close supervision before, during and after this treatment, and only preparations that have been tested for purity should be used. Hepatic and renal lesions and severe anemia are contraindications to this treatment. As an adjuvant the authors occasionally treated the anal area with a mixture of tumenol, zinc oxide and an anesthetic and prevented constipation. The treatment continues for two consecutive days and is repeated after three weeks. The authors used powders into which 1·25 Gm. of phenothiazine had been mixed. Children aged 2 to 4 years were given one powder a day, those 4 to 8 years two powders a day, those 8 to 13 years three powders a day, those 13 to 18 years four powders a day and adults six powders a day. A colorimetric determination of the excreted phenothiazine in the urine is described. One hundred and twenty-three patients were successfully treated. In 1 patient who had been given an overdose of the drug there developed hemolytic anemia.

DEFICIENCY DISEASES

WOODMAN, H. M. **Nutrition of the African in Tsetse-Fly Areas.** *East African Med. J.* 1947, Sept., v. 24, No. 9, 315–36, 1 pl. [35 refs.]

No scale of recommended dietary allowances has so far omitted meat and milk. Evidence is presented in this paper that these foods can, at least for the race and environment described, in which cattle cannot be kept because of tsetse, be satisfactorily substituted by non-animal foods, and the resulting diet lead to optimum health and development. The paper is modestly described as a " curtain-raiser " to some field nutrition survey work now being undertaken ; though qualitative, the observations, conclusions and recommendations will be found to have value far beyond the southern Sudan.

Foods.—Meat is only eaten at irregular intervals during a short hunting season. Fish, eggs and milk are rarely if ever used as food. The typical dietary consists of eleusine-manioc flour as a staple, with a wide variety of vegetables, roots, greens and fruit, ground-nuts, beans, oils and other cereals such as maize and rice. (A table of food values of common Sudan foods is given, including some new values.) It might be expected that such a diet would be deficient in high-grade protein, calcium and, seasonally, in vitamin C.

Nutritional Status.—The Africans of the southern Sudan are of fine physique, strength and stamina, and appear to have a high resistance to endemic diseases such as schistosomiasis and ankylostomiasis. The major deficiency diseases are not found. A few conditions attributable to malnutrition, such as xerosis, phrynoderma and " mosaic skin " are sometimes but not commonly seen, and three diseases, to the causation of which deficiency is probably contributory, are common—namely tropical ulcer, dental caries and leprosy.

Improvements in Nutrition.—The author puts forward suggestions for improvement of nutrition as part of a general scheme for raising the standard

of living. The scheme is formulated within the existing framework of social and agricultural customs and food habits. Measures directly concerned with food production include control of shifting cultivation and establishment of families in areas of up to 40 acres each; increased production and improved methods of preserving green vegetables; wider use of the soya bean; the use of food yeast; and the preparation of margarine in areas where vegetable oils are abundant. The author emphasizes, however, that these are only details in a development programme which is mainly economic, social and educational.

Dean A. Smith

JACQUES, J. J. C. Contribution au traitement du "Mbuaki" ou syndrome de dépigmentation du Kwango et du Kasaï. [**The Treatment of Mbuaki, the Syndrome of Depigmentation, in the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1947, Mar. 31, v. 27, No. 1, 73–82.

This is the latest of a valuable series of papers from the Belgian Congo on the disease known there as "diboba" or "mbuaki." [See VAN DAELE, this *Bulletin*, 1939, v. 36, 913; PIERAERTS, *ibid.* 1943, v. 40, 406; 1947, v. 44, 225; DOUCET, *ibid.* 1947, v. 44, 451.] It deals mainly with pathogenesis and treatment, the clinical picture having been adequately described by previous authors.

Treatment was directed primarily against the anaemia, which is one of the outstanding features of the disease. The results are summarized in 70 cases, all infants. All were treated with inorganic iron and anthelminthics. One group in addition received intramuscular injections of liver extract, and another—the largest—was given daily intraperitoneal injections of maternal blood, according to the method described by LODEWYCKS [*Rec. Travaux Sci. Méd. Congo Belge*, 1944, no. 2, 157]. In all three groups there was, in most cases, an increase in the haemoglobin level, as measured by the Talqvist method. The author makes the important point that the treatment of these patients in hospital may lead to mistaken conclusions about the result and mode of action of therapeutic measures. It is difficult to separate the effect of hospital diet and régime from that of drugs, and this invalidates the conclusions.

As regards pathogenesis, the author concludes that neither intestinal parasites nor malaria play an essential part in causing the disease, although both may aggravate it. The primary cause is a deficiency of protein and an excess of carbohydrate in the diet. In view of the response to iron, there is probably an iron deficiency, but avitaminoses are secondary.

[It is of interest that the workers in the Belgian Congo have reached the same conclusions about the cause of this disease as that derived from a study of similar cases many thousands of miles away in the West Indies (WATERLOW, this *Bulletin*, 1947, v. 44, 841; *Medical Research Council Spec. Rep. Ser., No. 263*, in the press). In both groups of cases, protein lack and carbohydrate excess have appeared to be the main causes, with vitamin deficiencies playing a secondary part. The Belgian writers have laid much stress on anaemia, which is not prominent in the West Indian cases. The latter, however, do not suffer from either malaria or intestinal parasites. This supports Dr. Jacques' view that these conditions are not of primary importance.] *J. C. Waterlow*

PASSMORE, R. **Mixed Deficiency Diseases in India: a Clinical Description.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Oct., v. 41, No. 2, 189–206. [37 refs.]

It has been pointed out by TROWELL [this *Bulletin*, 1946, v. 43, 1062] that the classical deficiency diseases are rare in Africa, whereas the effects of inadequate food intake are widespread. The same is true of India; beriberi, florid pellagra,

scurvy and rickets are seldom seen, but a symptom complex caused by varying degrees of mixed deficiency of total calories, protein, A and B-complex vitamins, and complicated by protozoal and helminthic infestations is distressingly common.

Though brief reference is made in this paper to the probable causation of individual manifestations by individual nutritional deficiencies, it is mainly devoted to a description of the over-all clinical picture seen in the common multiple deficiency state. There may be wide variation among individuals, the effects of one deficiency predominating or one system being mostly affected, but there is discernible in all cases a basic pattern which is substantially the same as that seen in Africa and other parts of the world.

General.—Loss of weight and listlessness are prominent early features. A profound depression and lack of the will to live may prove a serious obstacle in treatment.

The Skin.—Superficial hyperkeratosis with atrophy of the sebaceous and sweat glands produces a skin which is dry, rough and scaly, and which has a crazy-pavement appearance. Tropical ulcer is often associated with these changes, but the part played by nutrition in its aetiology is still uncertain. There is frequently involvement of the hair follicles, which gives rise to the distinct and characteristic follicular hyperkeratosis. Angular stomatitis, cheilosis and lesions of all muco-cutaneous junctions are attributed mainly to riboflavin deficiency.

The Eyes.—Xerophthalmia, keratomalacia and Bitot's spots with impaired dark adaptation (mainly avitaminosis A) are probably the commonest signs of malnutrition in India; superficial keratitis and nutritional amblyopia are common only in the south.

The Digestive System.—In most cases of malnutrition, glossitis and diarrhoea are present, the latter being the principal cause of death; general atrophy of the whole intestinal tract is usually seen at post-mortem examinations. Liver function in cases of malnutrition has been little investigated in India; in fatal cases, the liver is usually small and invariably fatty.

The Cardiovascular System.—There is usually evidence of cardiac atrophy with hypotension. Anaemia is usual, with some degree of macrocytosis; but the haematological picture is variable and probably represents the combined effects of nutritional deficiency and chronic malaria.

Treatment.—To secure a right psychological attitude and active co-operation is the first essential. This involves a cheerful ward, willing staff, attractive food and a certain pandering to the patients' whims. Milk is the standby in most cases. Vitamin preparations are of use in individual symptom-groups, but rarely achieve complete cure. Yeast products are of value, especially in out-patient work. The necessity for adequate treatment of co-existing infections and infestations is emphasized.

[Two printing errors have slipped in; their presence in no way diminishes the value of this excellent paper. On page 201 " . . . the value of vitamin A (aneurin) therapy . . . (next paragraph) Vitamin B_1 (thiamine) has been . . . " should obviously read " . . . the value of Vitamin A therapy. . . . Vitamin B_1 (thiamin or aneurin) has been. . . ." And the paragraph heading on page 203 " Treatment of Carcinoma Infections " should presumably read " Treatment of Concurrent Infections."] *Dean A. Smith*

BRAIN, W. R. **Malnutrition of the Nervous System.** *Brit. Med. J.* 1947, Nov. 15, 763–6, 4 figs. [39 refs.]

It has recently become increasingly apparent that a number of neurological disorders are related to defective diet or defective absorption of essential

nutrients. This relationship was the subject of a discussion at the Neurological Section of the International Congress of Medicine in September, 1947, when this was the introductory paper.

As befits an opening paper, it deals with the problems in general and slightly provocative terms ; it uses as examples chiefly the neuropathies recorded in prison camps during the second world war.

In the main, the discussion centres on the question : intoxication or deficiency ? ; and the difficulty of this apparently simple distinction is well exemplified in the cases of beriberi and arsenical poisoning. In the former, which is due basically to a dietary vitamin deficiency, the tissues may well be damaged by products of imperfect intermediary metabolism, in fact by local intoxication ; whereas in the latter, it has been shown that arsenite interferes with the pyruvate enzyme system and in arsenical poisoning the damage may be, in effect, due to local enzyme deficiency.

On somewhat parallel lines are discussed the aetiology of pellagra, Wernicke's encephalopathy, painful feet, the captivity cord syndromes and captivity cranial nerve lesions. *Dean A. Smith*

NICHOLLS, L. **Thiamine of Milled Raw and Parboiled Rice.** [Correspondence.] *Nature.* 1947, Aug. 30, 298.

It is known that a large part of the thiamin of wheat, rye, maize and barley is in the scutellum of the grain (59 per cent. of all the thiamin of wheat is in the scutellum), and it is probable that the same is true of rice. It has usually been assumed that when rice is parboiled, some of the thiamin is distributed from the germ into the whole grain, and that subsequent milling and removal of the germ does not, therefore, completely eliminate the thiamin. Nicholls, however, has examined milled parboiled rice grains and compared them with milled raw rice grains, and concludes that the effect of parboiling is rather to make the scutellum more adherent, so that in subsequent milling only part of it is removed, and therefore part of the thiamin is retained. With raw rice the whole germ is removed. Parboiling may cause some distribution of the thiamin throughout the grain, but its chief effect is probably retention of the scutellum. *Charles Wilcocks*

SPRUE

BLACK, D. A. K. & SIMPSON, J. A. **Serum Lipides in Tropical Sprue.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Oct., v. 41, No. 2, 241–54. [12 refs.]

Estimations of total fatty acid, lipide phosphorus and cholesterol were estimated in the serum of 16 patients suffering from tropical sprue and of 9 normal persons ; these were repeated at intervals after a standard meal containing 18 gm. of fat. The fasting level of total fatty acid in sprue did not differ significantly from normal values, but phospholipide and cholesterol were significantly lower. After a fatty meal, the total of fatty acids increased less in sprue patients than in normal persons ; but phospholipides showed a smaller increment than did neutral fatty acid. The cholesterol usually fell in sprue patients. No significant change was demonstrated in the fat curve after a period of liver treatment in four patients.

This low fat curve in sprue fits in well with the more direct evidence of faulty fat absorption given by stool analyses. The observed changes can be

well explained on the basis of STANNUS's hypothesis [this *Bulletin*, 1943, v. 40, 259] that the absorption defect affects only those lipides which are phosphorylated during absorption, but they cannot be said to prove it.

P. Manson-Bahr

ELDER, H. H. A. **Clinical Features, Diagnosis, and Treatment of Sprue.** *J. Trop. Med. & Hyg.* 1947, Nov., v. 50, No. 11, 212–18.

Four hundred cases of sprue were investigated and treated; all were in British soldiers. A table giving the place of origin shows that 75 per cent. arose in Bengal, Assam or Burma. This is shown below :—

Bengal, Assam and Burma	306
W. India	44
S. India and Ceylon	27
Central, North, North-West India and Overseas ...	23

The highest seasonal incidence in India, Assam and Burma was in May, June and July.

Long residence is not essential, as the following table suggests :—

Residence of 6 months–1 year	...	37 (9·25 per cent.)
,, 1–2 years	... ...	147 (36·75 per cent.)
,, 2–3 years	... ...	171 (42·75 per cent.)
,, Over 3 years	... ...	45 (11·25 per cent.)

Descriptions are given of the various clinical manifestations. For fat analyses, the patients were given, for three days, a diet containing about 23 gm. of fat, and a typical specimen of each stool passed during the three days was collected. An analysis was made of the mixture.

In 40 per cent. of cases, the total faecal fat was within normal limits, and it was shown that fully established sprue can persist in the absence of steatorrhoea. In a control analysis on the stools of 10 healthy men under the same conditions, the mean total faecal-fat was 29·3 per cent. of the dried stool, the maximum being 34·4 per cent. Out of the total :—

Glossitis was present in	393
Stomatitis was present in	212
Angular stomatitis was present in	177
Cheilitis was present in	62

The diagnosis and prognosis of the disease are discussed.

In treatment, sulphaguanidine (given in the acute stage) with an initial dose of 7 gm. and then 3·5 gm. every four hours up to a total of 60 to 70 gm. checked the diarrhoea and caused a marked improvement in the general condition. Liver was used in the treatment of anaemia and vitamin preparations for local lesions, with variable results.

Detailed clinical notes of four cases are given. Four diet schedules are set out in an appendix.

P. Manson-Bahr

WEIR, J. F. & COMFORT, M. W. **Folic Acid Therapy in Nontropical Sprue: Results of Treatment in Seven Cases.** *J. Lab. & Clin. Med.* 1947, Oct., v. 32, No. 10, 1231–41.

These seven cases have been worked out in great detail, and no useful purpose can be served by summarizing all the data.

Control data were collected before institution of treatment, and special attention was paid to the frequency, duration and severity of the exacerbations, including frequency and character of stools. Haematological studies included

sternal puncture. The concentration of calcium, phosphorus, total protein, albumin and globulin in the serum, as well as values for phosphatase and prothrombin times, were determined. X-ray examination of the skull, hands and teeth for osteoporosis, as well as of the small bowel for the so-called deficiency pattern, was secured. In four subjects the faecal solids, fats and nitrogen were determined daily during a three-day test period.

Vitamins, including sufficient vitamin K to control hypoprothrombinaemia, were given. The dosage of folic acid usually was 50 mgm. daily by the intramuscular route.

Treatment with folic acid did not result in improvement in the sense of well-being, gain in weight or strength that could not be equally well accounted for by increased intake of food, and natural remission of the disease. Frequency or severity of exacerbation of the intestinal manifestations did not change. Moreover, the haematological response was disappointing. All these points are in marked contrast to the favourable responses of tropical sprue to folic acid. Whether the two conditions are different, or whether these cases had advanced to an irreversible stage is impossible to state. *P. Manson-Bahr*

HAEMATOLOGY

FINDLAY, G. M., BOULTER, E. A. & MACGIBBON, C. B. **A Note on Sickling and Flying.** *J. Roy. Army Med. Corps.* 1947, Sept., v. 89, No. 3, 138–41.

"Experiments were carried out in West Africa to determine whether a flight up to 15,000 feet above sea level, without administration of oxygen, would induce an acute haemolytic crisis in Africans with sicklaemia.

"Three Africans with sicklaemia showed no ill-effects from such a flight, although all showed the presence of sickled red cells at 15,000 feet above sea level after ten to fifteen minutes at this height.

"Differences in the rate at which sickling occurred *in vitro* in different individuals were noted and are correlated with the *in vivo* findings."

BENAIM PINTO, H., CARBONELL, L., GIL, J. A. & GÓMEZ, O. L. Primera descripción de la anemia drepanocitica en Venezuela. [**First Record of Sickle-Celled Anaemia in Venezuela.**] *Rev. Policlinica Caracas.* 1947, Jan.–Feb., v. 16, No. 92, 1–29, 7 figs. [25 refs.]

A very detailed report of a case.

EPIDEMIC DROPSY

MITRA, K. & RAO, K. K. P. N. **Investigations into an Outbreak of Epidemic Dropsy.** *J. Indian Med. Ass.* 1947, June, v. 16, No. 9, 303–6.

The authors were called upon to investigate a "sudden outbreak of bowel complaints associated with swelling of the extremities." [No dates or names of places affected are stated, so the report is deprived of much of its value as a historical record.] Four hundred and fifty-eight persons were affected out of a total of 794, the adults being railway employees. The diagnosis rested between beriberi and epidemic dropsy. None of the patients was under

8 months of age ; the percentage of infected rose from 17 (8 out of 47) below two years of age, to 65·7 (136 out of 207) adult females and 75·5 (173 out of 229) adult males. Investigation traced the source to mustard oil purchased at the railway provision store. As some time had elapsed since the start of the outbreak, only nine samples of the mustard oil could be collected ; six of these gave the Argemone oil reaction of LAL and his colleagues. The symptoms were typical : Abdominal pain and discomfort, flatulence, diarrhoea for 3–5 days, occasionally more, followed by swelling of the legs. In a few patients the swelling of legs preceded the diarrhoea. Palpitation and shortness of breath were also complained of. The interval between obtaining the oil and the onset of symptoms ranged between 9·3 and 15·6 days, with an average of 11·3. The outbreak died down rapidly when issue of the oil from the store was stopped. *H. Harold Scott*

DERMATOLOGY AND FUNGUS DISEASES

KERVRAN, P. & ARETAS, R. Deux cas d'histoplasmose observés au Soudan français. [**Two Cases of Histoplasmosis seen in the French Sudan.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 7/8, 270–76. [11 refs.]

[The two cases described in this paper are the same as those noted in this *Bulletin*, 1947, v. 44, 1018. These cases, and two cases of histoplasmosis from tropical Africa identified by the reviewer in 1943 and 1946 respectively—the only authentic cases of the disease so far reported from this part of the world—all showed the larger form of *H. capsulatum* in the lesions.] *J. T. Duncan*

EMMONS, C. W., BELL, J. A. & OLSON, B. J. **Naturally occurring Histoplasmosis in *Mus musculus* and *Rattus norvegicus*.** *Pub. Health Rep.* Wash. 1947, Nov. 14, v. 62, No. 46, 1642–6. [14 refs.]

In a previous paper [this *Bulletin*, 1947, v. 44, 848], the authors reported the discovery of histoplasmosis in a house mouse (*Mus musculus*) during an investigation on the occurrence of the disease in an area of Loudoun County, Virginia. The present paper deals with the continuation of this investigation and records the discovery of histoplasmosis in 10 wild rats (*Rattus norvegicus*) trapped on three different farms. It is noteworthy that the infected animals showed no macroscopic sign of the infection and they were detected only by cultivation of *Histoplasma capsulatum* from their tissues ; chiefly the liver and spleen. This, the first recorded discovery of naturally acquired histoplasmosis in wild rodents, constitutes a very important advance in the elucidation of the puzzling epidemiology of the disease ; albeit the infection is not known to be transmitted directly from animal host to animal host.

Additional observations were the discovery of *Blastomyces lanuginosa* in one mouse, and a species of *Cryptococcus*, pathogenic for experimental animals, which was isolated from 81 animals, chiefly rats and mice. *J. T. Duncan*

KURZ, E. R. H. & LOUD, N. W. **Coccidioidomycosis in New England.** *New England J. of Med.* 1947, Oct. 23, v. 237, No. 17, 610–16, 5 figs. [21 refs.]

A discussion of four cases in returned servicemen.

HEAT STROKE AND ALLIED CONDITIONS

MARRIOTT, H. L. **Water and Salt Depletion.** *Brit. Med. J.* 1947, Feb. 15, Mar. 8 & 15, 245–50 ; 285–90 & 328–32, 10 figs. [122 refs.]

(The Croonian Lectures, delivered at the Royal College of Physicians, London, December, 1946).

Water and salt are, perhaps, the most important substances it is in our power to administer in a wide variety of clinical conditions. They can be so used as to achieve seeming miracles ; or so misused as to lead to avoidable fatalities. The effects of water and salt depletion have commonly been confused ; recent experimental and clinical work have made it possible to recognize with certainty the separate effects and to treat them on sound physiological lines.

In the present paper, the author presents a lucid and immensely valuable summary of the whole subject.

Among the important physiological considerations vital to the understanding of water and salt depletion are :—

(1) The distribution of body fluid between the intracellular (about 35 litres in an adult man) and extracellular (about 14 litres) compartments.

(2) The subdivision of the latter into plasma (about 3 litres) and tissue or interstitial fluid (about 11 litres), and the constant to-and-fro filtration which occurs between them, governed by hydrostatic pressure and by the colloid osmotic pressure of the plasma protein.

(3) The necessity for maintaining osmotic isotonicity of the tissue fluid as the " internal environment " of cells, distribution of water between cellular and tissue fluids being determined by the osmotic pressure of electrolyte ions.

(4) Renal regulation of extracellular fluid osmotic pressure by selective reabsorption of components of the glomerular filtrate.

(5) The magnitude of the daily " unavoidable " loss of water by vaporization (lungs and skin, 1,000 ml.) and as the minimum urine volume for excretion of waste products (500 ml.).

Pure water depletion occurs when water intake stops or is greatly diminished and when there is no significant sodium chloride loss in secretions. It may be caused by deprivation of water as in shipwreck, or by inability to swallow as in severe dysphagia, great weakness or coma. The extracellular fluid becomes hypertonic because water is lost without parallel salt loss, water is sucked from the cells, extracellular fluid volume tends to be maintained and dehydration is principally cellular.

Pure salt depletion occurs when there are abnormal losses of sodium and chlorine in the presence of adequate water intake. It may arise in severe vomiting or diarrhoea from any cause, continuous gastro-intestinal suction drainage, biliary or intestinal fistulae, Addison's disease or, most characteristically, in " heat exhaustion " (severe sweating accompanied by free drinking of unsalted fluids). The osmotic pressure of the extracellular fluid falls and the kidneys excrete water to maintain its isotonicity. This leads to diminution of extracellular fluid volume—secondary dehydration. There follows the condition of oligaemic circulatory failure or " shock ", and death is due to decreased blood volume and increased blood viscosity. There may be, as a secondary effect, disturbance of the acid-base balance when there is asymmetrical loss of sodium or chlorine ions, *e.g.* alkalosis in severe vomiting and acidosis in diarrhoea (as in cholera).

The effects of water and salt depletion are compared in the following table :—

Manifestation	Pure Water Depletion	Pure Salt Depletion
Dehydration	+++ primary or simple	+++ secondary or extra-cellular
Thirst	+++	Absent
Lassitude	+	+++
Orthostatic fainting	Absent till late	+++
Urine volume	Scanty	Normal till late
NaCl in urine	Often +	Always absent (except in Addison's disease)
Vomiting	Absent	May be +++
Cramps	Absent	May be +++
Plasma NaCl	Slight increase or normal	Greatly decreased
Blood urea	+	+++
Plasma volume	Normal till late	Greatly decreased
Haemoconcentration	Not till late and slight	+++
Blood viscosity	Normal till late	Increased +++
Blood pressure	Normal till late	Fall +++
Water absorption	Rapid	Slow
Mode of death	? due to rise of osmotic pressure	Peripheral circulatory failure

Adequate treatment depends not only upon an accurate qualitative diagnosis, but on an estimate of the quantitative extent of the deficiency in terms of deficit of water or of isotonic saline ; either may be as high as 10 litres. In this connexion and in control of treatment the simple and rapid method of FANTUS (*J. Amer. Med. Ass.*, 1936, v. 107, 14) for estimating chloride in urine is invaluable (details of technique and interpretation are given and may also be found in this *Bulletin*, 1944, v. 41, 74).

Treatment.—In water depletion, water should be given by mouth or per rectum unless circumstances compel parenteral administration, in which case isotonic glucose solution (5 per cent.) is the best vehicle for the water. In salt depletion, isotonic saline solution should be used until symptoms are relieved or until chloride reappears in the urine, when it should be replaced by hypotonic ($\frac{1}{2}$ to $\frac{1}{3}$ isotonic) saline. The aim should, in either case, be to achieve a minimum urine volume (in an adult) of 1 pint per 8 hours with a salt content of 3 to 5 gm. per litre.

An adult suffering from any significant degree of either water or salt depletion will need to receive within the first 24 hours at least a gallon ($4\frac{1}{2}$ litres) of appropriate fluid. *Dean A. Smith*

TROPICAL ULCER

GUTCH, C. F. **Local Penicillin Therapy for Tropical Ulcer.** *U.S. Nav. Med. Bull.* 1947, Sept.–Oct., v. 47, No. 5, 801–4, 1 fig.

The author estimated that about half of the Chinese coolies in a camp in Szechwan Province suffered from tropical ulcer. The hygienic conditions of the coolies were bad, undernourishment was rife, malaria and tuberculosis were common and parasitism was almost invariably present.

The ulcers were readily differentiated and they followed in general the classical descriptions, with spirochaetes, fusiform organisms and secondary

bacteria. The usual lengthy series of treatments were tried with varying degrees of success, but it is noted that local applications of sulphanilamide powder produced some measure of success in several cases. Initial therapy consisted of cleansing the affected limb with soap and water, irrigation of the ulcer with hydrogen peroxide and saline, and removal of as much necrotic tissue as possible.

Owing to inadequate response of the ulcers to other forms of treatment, local penicillin was applied to some of them, after initial cleansing. Dry penicillin sodium (100,000 to 200,000 units) was sprinkled over the surface, which was then covered with gauze impregnated with vaseline: this confined the concentrated solution of penicillin (the penicillin dissolved rapidly in the serum of the wound) to the area having most organisms. The patients were seen daily and further applications of penicillin were made if necessary.

In 32 of 35 ulcers so treated, granulation tissue assumed a healthy appearance and peripheral induration diminished significantly in 24 to 72 hours. When the wound became clean, it was kept so with sulphanilamide powder and dry dressings. In the three more resistant cases, similar results were achieved after 5 to 6 days treatment with penicillin. Most of the patients experienced a local burning after the application: this disappeared in a few minutes, and was the only ill-effect noted.

Details are given of one case in which satisfactory results with penicillin, followed by sulphanilamide, were obtained, so that on the 10th day "pinch" grafts could be placed on the granulations. The patient had been working throughout the treatment and continued to do so: despite ambulation, all the grafts took and within three weeks thereafter epithelialization was complete. [See also this *Bulletin*, 1946, v. 43, 958; *ibid.*, 1947, v. 44, 748, 935.]

H. J. O'D. Burke-Gaffney

MISCELLANEOUS DISEASES

MacCreary, D. & Bricker, A. G. **The Incidence of Intestinal Parasites among Civilians emplbyed at certain Naval Air Bases.** *U.S. Nav. Med. Bull.* 1947, Sept.–Oct., v. 47, No. 5, 926–9.

When Parnamarim Field, Natal, Brazil was being surveyed for anti-malarial purposes in 1943, the authors noted that latrine facilities for the hundreds of native labourers were lacking and that heavy faecal pollution of the neighbouring scrub brush was taking place.

Many stools showed evidence of diarrhoea and a preliminary examination of direct smears from 15 fresh stools produced startling results: nine species of intestinal parasites were found, each sample contained at least one species and one contained no less than six. Seven of the fifteen showed *E. histolytica*. The full results are shown in a table.

Examinations were therefore made of waiters and dish washers. Similar stool examinations were made at Pici' Field, Fortaleza, some 200 miles to the north of Natal, and at Aratu seaplane base and Ipitanga Field, both within 25 miles of Bahia and approximately 30 miles apart, and some 450 miles to the south of Natal.

A total of 133 examinations are recorded from Natal (61), Fortaleza (44), Aratu (15) and Ipitanga (13).

Although only one stool was obtained from each person and no concentration methods were used, not one parasite-free sample was obtained.

Among other findings revealed in a table are that hookworm had the highest incidence, accounting for 71 per cent. for the whole group (although Aratu seaplane base produced 93 per cent. of *Ascaris*). *Ascaris* accounted for 62 per cent. for the whole group. *E. histolytica* varied from none at Ipitanga to 27 per cent. at Fortaleza and *E. coli* averaged 37 per cent. *Strongyloides* occurred in 13 per cent. and the other common parasites in lesser degree.

Schistosoma mansoni was found once at Fortaleza, twice at Aratu and three times at Ipitanga: it was not found at Natal, where conditions appear to be unfavourable for *Planorbis*.

The authors note the difficulties in avoiding the ingestion of parasites in such an area and the need for rigid precautions to avoid contamination of food and water. Despite the small series, the investigation does represent a segment of conditions in four areas extending some 850 miles along the coast. Although unusual care was taken, one of the authors acquired *E. histolytica* and *Ascaris* infections: it is observed that long intervals without fresh vegetables will cause a normally cautious person to "take a chance". *H. J. O'D. Burke-Gaffney*

DAVIES, J. N. P. **Pathology of Central African Natives. Mulago Hospital Post Mortem Studies Series III.** *East African Med. J.* 1947, Aug., v. 24, No. 8, 289–303. [26 refs.]

Lobar pneumonia has long been recognized as accounting for a high proportion of deaths amongst Africans. VINT, in Nairobi, [*East African Med. J.*, 1928, v. 5, 383] found it responsible for death in 42 per cent. of post mortems he performed in one year, and in 1937 [*ibid.*, v. 13, 332] reported finding the disease in 29·8 per cent. of 1,000 consecutive autopsies, the right lung being predominatingly affected. GARNHAM and DE SMIDT [*ibid.*, 1931, v. 8, 150], typing pneumococci from 100 cases in Africans, found Type IV in 91 per cent., ORMISTON in England (1942) found this type in England in 61 per cent.

In 2,994 autopsies performed at Mulago, Uganda, lobar pneumonia was found in 15·7 per cent., more persons dying from this condition than any other. Bacteriological examination of 170 cases showed pneumococci in 90 per cent., but right lung involvement was not nearly so marked as in Nairobi. There is no evidence that the disease is more severe than in England; possibly it is even milder. Most of the deaths appear to have occurred in the third decade of life.

Of the 472 cases recorded 37 per cent. showed complications due to the infection (*cf.* VINT, 1937 *loc. cit.*, who reported 26·2 per cent. in Nairobi). These were as follows:—

Group 1.	Local complications in the lungs ...	43 cases (9·1 per cent.)
I.	Suppurative softening (small abscesses)...	3 cases (0·6 per cent.)
II.	Abscess	33 cases (6·9 per cent.)
III.	Gangrene of lung (all lower lobe) ...	8 cases (1·7 per cent.)
IV.	Delayed resolution and carnification ...	15 cases (3·1 per cent.)

Group 2. Direct spread from lung.

Only one case of subphrenic abscess and one of suppurative mediastinitis were noted. Empyemata were found in 43 instances (9·1 per cent.) and of 14 cases examined bacteriologically, pneumococci were found in 13, staphylococci in one. Pericarditis occurred in 39 (8·1 per cent.), 23 being purulent; there was no evidence that this was usually associated with right lung involvement. In only 2 per cent. of the empyema cases were there septicaemic complications.

Group 3. Septicaemic complications.

Meningitis: 16 (3·3 per cent.); 12 of 13 cases were pneumococcal and 1 meningococcal.

Endocarditis : 15 (3·1 per cent.) ; 9 out of 10 cases examined being pneumococcal and 1 due to *Haemophilus influenzae*. Septicaemic signs without localization were found in 4 cases. One interesting complication was pneumococcal encephalitis—recognized in 12 cases. At autopsy, lobar pneumonia was found, the meninges being slightly hyperaemic but without exudate and with sterile cultures ; the brain was hyperaemic and in some cases large punctate haemorrhages were found. Portions of the brain removed and injected intracerebrally into animals failed to show a virus, but the animals died of pneumococcal meningitis. Peritonitis was found in 6 cases.

The above figures are analysed and compared with those of Osler & Macrae, and Vint, in a table in the text.

Of 253 cases of broncho-pneumonia 40 were apparently primary, 26 secondary to enteric fever, 35 showed marked malnutrition, 40 had syphilis and 29 tuberculosis : 22 cases occurred in children. Malnutrition and gross structural changes, *e.g.* cirrhosis of the liver, are considered to play an important predisposing part in pneumonia, the so-called "tropical diseases" a relatively unimportant one.

The question whether pyogenic infections are more common in Africans than in Europeans requires further surveys, but some differences are apparent. Firstly streptococcal infections in Africans are relatively rare and harmless (at any rate in Kampala) ; this is not the case in Europeans [the reviewer has found the Masai, living mostly on blood, milk and meat, to have a high apparent degree of immunity to this infection.] The pneumococcus shows a greater tendency in Africans to cause septicaemia without lung involvement.

What evidence there is available suggests that the incidence of lobar pneumonia is high in Africans ; but here it must be remembered that the records come mostly from people herded together in towns, industrial areas etc., *i.e.* away from their normal environment, and that the disease is most common in newcomers. The probability is that, in his normal habitat, the African acquires immunity only to those types common in his district. The theory that blockage of the reticulo-endothelial system is responsible for the frequency of septicaemia is hard to accept, and it is difficult to see what infections are to blame ; the spleen of many Africans is fibrosed (because of malaria) but much of the reticulo-endothelial tissue lies outside this organ.

It is thought that increased susceptibility to septicaemic and pyogenic disease lies mainly in two causes.

(1) Malnutrition (very common). (2) Poor economic conditions, *i.e.* severe labour, liability to constant abrasions and ulcerations of the skin, poor housing, exposure to cold and wet, all give more opportunity to infection than in Europeans.

[It is a truism to say that more than half the problem of improving the general health of the African lies in better feeding, especially with proteins of high biological value.] [For Parts I and II of this series, see this *Bulletin*, 1947, v. 44, 1098.] *C. F. Shelton*

PROTOZOOLOGY : GENERAL

SPENA, A. Contributo allo studio della toxoplasmosi e considerazioni sulle diverse specie che costituiscono il genere *Toxoplasma*. [**Species of** *Toxoplasma*.] *Riv. di Parassit.* Rome. 1947, June–Sept., v. 8, Nos. 2/3, 85–104, 6 figs. [19 refs.] English summary (3 lines).

Toxoplasmosis was observed in laboratory guineapigs in Addis Ababa. The infection was inoculable from guineapig to guineapig, as also to the rabbit and

a calf. The parasites occurred in all the organs. The author discusses the identity of the parasite in relation to *Toxoplasma caviae* Carini and Migliano, 1916, and concludes that it is better to consider that a single species exists which would be *T. gondii* Nicolle and Manceaux, 1919. *C. M. Wenyon*

ENTOMOLOGY AND INSECTICIDES : GENERAL

KAHN, M. C. **Females Mosquito " Calls " and their possible Significance in Control.** *Kuba.* Habana. 1947, May, v. 3, No. 5, 119–20.

In this short article the author describes how he made recordings of the sounds produced by the females of the following mosquitoes : *Anopheles quadrimaculatus*, *Aëdes aegypti*, *Aëdes albopictus* and *Culex pipiens*. The records were made in a sound-proof chamber kept at atmospheric conditions comparable with those in the natural environments of the insects. He states that " most of the significant sounds are made while the insects are at rest " and are in the range of from 200 to 8,000 cycles per second. The recordings are not audible to the human ear ; they " require to be amplified some one-hundred million times or more ". He claims, however, that an experienced observer can distinguish the sounds of one genus or species from another and can also distinguish the sounds made by the sexes of the same species. When a record of a female voice is played, males of the same species fly towards it ; the author therefore hopes to transfer the sounds to magnetic tape for continuous playing and to test its ability to lure males to an electrical device which will kill them. [See also this *Bulletin*, 1945, v. 42, 661.] *H. S. Leeson*

GRENIER, P. Facteurs écologiques conditionnant la répartition des larves de *Simulium* (*Dipt.*). Variations morphologiques spécifiques en rapport avec la vitesse du courant. [**Ecological Factors affecting the Distribution of *Simulium* Larvae : Specific Morphological Changes related to Rate of Flow of Water.**] *C.R. Acad. Sci.* 1947, Nov. 10, v. 225, No. 19, 901–3, 1 fig.

MOOSER, H. Das synthetische Insektenmittel DDT. [**The Synthetic Insecticide DDT.**] *Wien. klin. Woch.* 1947, Nov. 28, v. 59, No. 47, 773–7. [14 refs.]

A general review.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

BARRETT, R. H. **Health Regulations for Air Travel.** *Brit. Med. J.* 1947, Nov. 8, 741–3. [Summary appears also in *Bulletin of Hygiene.*]

The rapidity of air transport at the present time has greatly increased the difficulties of health authorities throughout the world in view of the lack of clinical signs of infectious disease to be expected among the passengers examined. It is necessary, therefore, to place more reliance on immunization, and hence it is insisted that vaccines of known efficiency should be used and that the passenger should produce proof, in the form of certificates, that the operation has been performed satisfactorily.

The author has discussed briefly the methods of control and the regulations in force against the five major epidemic diseases, yellow fever, smallpox, cholera, plague and typhus.

In Table I are listed the accepted incubation periods of these diseases, and the periods of validity of the certificates of immunization agreed on internationally.

TABLE I

Disease	Incubation Periods	Periods of Validity of Certificates of Immunization
Yellow fever	6 (India 9) days	For 10 days to 4 years from date of inoculation
Smallpox	14 days	For 14 days to 3 years from date of vaccination
Cholera ...	5 days	For 6 days to 6 months from date of inoculation
Plague ...	6 days	Not stated, but usually for 6 months from date of inoculation
Typhus ...	12 days	For 1 year from date of completion of course of inoculations

Inoculation and Vaccination.—The number of inoculations or vaccinations required by a particular passenger depends on the route on which he will fly. It will be necessary for him to comply with the regulations of each country in which he lands as well as those of the country of departure and of his destination. The regulations, however, usually make a distinction for a passenger who is only in transit through a country and not disembarking into it, and in the former case an alleviation of the rules is sometimes permitted. Health authorities are naturally anxious to prevent the entry of a person incubating any disease into a country where conditions are particularly favourable for its spread. This is the case in India, where regulations against the importation of yellow fever are very stringent in consequence of the presence of *Aëdes* mosquitoes. Similarly, in Australia, special precautions against smallpox are insisted on.

Variation in Validity of Immunization Certificates.—The periods of validity of certificates of inoculation and vaccination as shown in Table II vary in certain countries, and it is necessary to ensure that each passenger is in possession of certificates that are valid for all countries in which he will land during his journey. It would, of course, simplify the procedure for passengers if all countries would agree to accept the same periods of validity.

TABLE II

Disease	Convention Validity	Limits of Variation*	
		Maximum	Minimum
Yellow fever	10 days/4 years	15 days/2–4 years (India)	15 days/2 years (Madagascar)
Smallpox ...	14 days/3 years	21 days/2 years (Egypt)	12 days/1 year (Thailand)
Cholera ...	6 days/6 months	14 days/6 months (Abyssinia)	6 days/3 months (Hong Kong)
Plague ...	None stated	5 days/2 years (Cyprus)	6 days/3 months (Hong Kong)
Typhus ...	—/1 year	12 days/1 year (Lebanon)	8 days/6 months (Cyprus)
Typhoid ...	None stated	6 days/1 year (Burma)	6 days/3 months (Java)

*Calculated from date of completion of inoculation or of vaccination.

It is important that the passenger and practitioner should take into account the interval of time that must elapse before the certificates of these operations become valid. These periods are referred to in Tables I and II. The

consequences to a passenger who is not in possession of the requisite certificates may be a refusal of permission to embark, an enforced period of quarantine at the port of disembarkation, or refusal of permission to land.

In general, vaccination against smallpox and inoculation against the typhoid group should be recommended to any person proceeding abroad. Other inoculations need be advised only when epidemics are known to be in progress.

If the methods employed to control the entry of disease into countries by air appear to assume an importance not hitherto known in sea or land transport, it should be remembered that practically all international flights are, from the point of view of quarantine, well within the incubation period of the major epidemic diseases.

All materials for these inoculations, except yellow fever vaccine, are available for use by practitioners. The yellow fever vaccine must be kept under more exact conditions and so is only available for inoculation in certain centres which are listed.

A brief description of health regulations affecting aircraft and crew is also given. *F. O. MacCallum*

WORTHINGTON, E. B. **A Development Plan for Uganda.** With a Foreword by His Excellency the Governor of Uganda, Sir J. Hathorn HALL. pp. xii+112, 10 figs. (8 maps). 1946. Dec. Entebbe: Govt. Press. [Shs. 2/50.]

At the present time there is a strong movement to develop the economic and social life of the countries of Africa, and a growing realization that if this is not undertaken thoroughly, and soon, the people will shortly be faced with famine because their agricultural habits are not adequate to keep pace with a rapidly increasing population. At the same time there is the realization that although much is known about the economic potentialities of these countries, much remains to be discovered before any rational plan of progress is possible. The present volume is the outcome of a study of the problems inherent in any scheme of development. Dr. Worthington's wide knowledge and experience have enabled him to correlate the different sides of the subject, and to formulate proposals.

He discusses the matter under various headings :—The fundamental problem, finance, the productive services, social services, the common services, and special developments. The chief and most stubborn fact of the fundamental problem is that the present population of about 4,000,000 is likely to increase to 10,000,000 in the next 50 years, and that the productive capacity of the soil will then be used to its fullest extent, if all suitable land is made available. At present the land is not all available, but much more could be worked if, for instance, lack of water was made good. The country could support this enlarged population if the output per person were increased, and if the large areas now unused were rendered usable.

This plan cannot satisfactorily be summarized, and readers are referred to the original for details of the many enquiries made and opinions expressed. The author has received much assistance from those who have worked in Uganda, and studied its problems, for many years. *Charles Wilcocks*

KALRA, S. L. **Addu Atoll (Maldive Islands) its People and its Important Diseases.** *J. Indian Army Med. Corps.* 1947, July, v. 3, No. 3, 137–41.

The Maldive Islands are atolls, rising no more than a few feet above sea level ; the soil is mainly soft coral sand, rich in lime. Vegetation is abundant, and palms, plantains, breadfruit, papayas, sweet potatoes and other bulbous roots grow prolifically ; the growth of scrub is very thick. Swamps, some of sweet water, abound, and fresh water is easily obtained from shallow wells. The

average rainfall is 66 inches per annum. The author describes the conditions of life, which have already been recorded by MANSON [this *Bulletin*, 1946, v. 43, 1202].

The common diseases are scrub typhus, malaria, filariasis and dysentery. The only *Anopheles* is *A. tessellatus*, which breeds solely in wells of fresh water; it has been found infested in nature. The range of flight of *A. tessellatus* is more than half a mile but less than two miles. In wells containing small fish (*Barbus* spp.) no mosquito larvae could be found. Spleen rates are fairly high. Culicine mosquitoes are abundant.

Scrub typhus is probably carried by *Trombicula deliensis* in these islands; the local people are apparently immune, and cases have been found only in the garrison. Filariasis is due to *Wuchereria bancrofti*, and both *Culex fatigans* and *C. sitiens* have been found infected. Filariasis is present in all villages.

Ulcers of the legs, due to secondary infection of injuries from coral, are fairly common.

Charles Wilcocks

PEARSE, A. S. [Edited by]. **Zoological Names. A List of Phyla, Classes, and Orders.** Prepared for Section F American Association for the Advancement of Science. 22 pp. 1947. Durham, North Carolina.

A second edition of this list, which was first issued in 1936 and which has been out of print for several years, has now been published. In this, a number of corrections have been made. The list does not go beyond suborders.

In his preface to the first edition, the editor discusses some of the difficulties attending any effort to achieve uniformity in zoological nomenclature, and admits that he has been unable to do so. He names the large number of experts who have advised him on the nomenclature adopted in the various sections. Two columns are given on each page, the first comprising the names (with authors and dates) which the editor, after consultation, believes to be in best current usage; the second containing the names which "a few zoologists would like to see used". The following endings are adopted:—Phylum and Subphylum, -a; Class, -ea; Subclass, -ia; Order, -ida; Suborder, -ina.

This is a most useful reference list, which will help zoological teachers and students (including medical men interested in tropical diseases) to avoid some of the confusion which now exists in zoological nomenclature.

Charles Wilcocks

BOOK REVIEW

BLACKIE, W. K. [M.D., Ph.D., F.R.C.P. (Ed.), D.T.M. & H., Hon. Consulting Physician, Salisbury Hospital, Southern Rhodesia, etc.]. **Malaria, with special reference to the African Forms.** 101 pp., 44 coloured figs. on 1 pl. 1947. Cape Town: Published for the Post-Graduate Press by the African Bookman. [10*s.* 6*d.*]

This monograph on malaria is the first book to be published for the Post-Graduate Press of Cape Town with the aid of a grant from Messrs. Bayer Pharma Ltd. It is written from the point of view of the general practitioner and specially for those working in Africa; it is for the latter reason that the book has a particular value. None of the standard text-books on tropical medicine, nor the earlier monographs on malaria, gives quite such a clear

picture of those forms of the disease encountered in tropical and Southern Africa. No one has yet demonstrated the exact nature of the differences that exist between African and classical malaria and the author makes no claim to have done so, though he takes the generally accepted view that strains of parasites and the degree of immunity in the indigenous population are important factors. He also points out that the high order of premunity prevailing among the adult population calls for a very different approach to the diagnosis of any acute fever.

The book comprises a clear account of the parasitology and pathology of malaria, the clinical features and treatment. It is confined to human forms of the disease, and it does not include within its scope a description of the anopheline vectors, epidemiology, or of measures of control. There is a coloured plate which gives an adequate picture of the various species of malarial parasites, though it omits the degree of magnification and the method of staining, and it includes *Plasmodium tenue*, a parasite which is not mentioned in the text.

The author adopts the unusual clinical classification into the following forms :—

In Europeans :

1. Acute benign malaria—due to *P. vivax*, *P. ovale* or *P. malariae*.
2. Acute malignant malaria—due to *P. falciparum*.
3. Chronic malaria.

In Africans.

1. Acute malaria—due to any species.
2. Chronic malaria.

This classification may be of value to the practitioner, but it leads to some overlapping in the description of the clinical features, and its use must tend to the ignoring of species diagnosis which is the only rational approach. A more serious defect is the division into European and African forms of the disease—the division should be into susceptible races and relatively non-susceptible races. Many Africans (*i.e.*, adult Africans) come into the former category and their disease syndromes are identical with those of Europeans. A proper understanding of this problem can only be reached after prolonged study of the nature of immunity and this, unfortunately, is dealt with very sketchily. A book which is written with special reference to the African forms surely deserves more than a page and a half on this subject.

A full account is given of the clinical features and of the different pernicious forms of *P. falciparum* malaria. Blackwater fever is not included in this monograph. Some of the statements which echo from text-book to text-book are again repeated here ; their accuracy is doubtful and their importance is magnified. To begin with ,this emphasis on the protean manifestations of the disease is very little justified. Ross [above, p. 141] has recently pointed out the dangerous error of regarding malaria in this way ; in the vast majority of cases, it is a simple illness easily recognized, and diagnosed for certain by finding parasites in the blood. Again, how valid are all these different forms of pernicious malaria, algid, hemiplegic, bulbar, hyperpyrexial, gastric, dysenteric, pneumonic, sudoral, etc.? How often are these in reality meningococcal meningitis, a virus encephalitis, a bacillary dysentery, heat stroke, etc.? Lastly may be mentioned the statement that is so often read, and for which there is so little evidence, that the infant mortality from malaria amongst African children is heavy. As Sir Leonard Rogers (*Fevers in the Tropics*) has pointed out, when such deaths are more closely investigated, the true figure gets lower and lower (*e.g.*, from 90 per cent. to 20 per cent.).

In the chapter on diagnosis, the author recommends the use of Giemsa's stain and of Field's rapid method. It is an advantage to become complete master of one or two methods ; nevertheless a description of Leishman's stain might have been added, and the J.S.B. rapid stain [this *Bulletin*, 1944, v. 41, 822] is superior in many ways to Field's. It is strange to find sternal puncture included in aids to diagnosis, whilst the much more useful—and therapeutically valuable—method of adrenaline provocation (of Ascoli) is omitted.

In regard to treatment, both curative and prophylactic, the author recommends the current standard procedures. He takes a commonsense view on the use of injections ; if the patient cannot absorb the drug by the oral route, then parenteral administration is necessary. In one place, the author gives the curative dosage of mepacrine as 0·3 gm. a day (p. 81), in another 0·3 gm. thrice daily (p. 93) : apparently he means the former. All the dosages recommended are perhaps slightly on the high side (*e.g.*, quinine 30 grains daily for approximately 5 days, followed by 0·3 gm. mepacrine daily for 5 days). Not many patients would consent to stay in bed for 3 or 4 days after the temperature has become normal. The author follows the lead of Marchiafava and other Italian physicians in stressing the importance of lumbar puncture in the therapeutics of cerebral malaria.

The danger of becoming over-enthusiastic in regard to a new form of treatment is well illustrated in this book, in the case of paludrine. Fortunately, the author had time to insert an addendum, stating that this drug fails to bring about the rapid control of African fevers as claimed in the original publications and that severe attacks of malignant malaria have occurred in spite of systematic paludrine prophylaxis.

The book as a whole is full of interest, is well presented and contains few mistakes. The above criticisms of the reviewer are largely on matters of opinion on a subject which is so prone to dogmatism. Genuine mistakes do occur—for instance—the statement that the " various members of the genus (Plasmodia) " (p. 9) develop in the female anopheline mosquito—instead of in various genera of mosquitoes. Matters of opinion are illustrated by assertions such as " hepatic tenderness is almost invariably present " (p. 40) in acute malaria. This is perhaps true in Southern Rhodesia where the author works, but it may not be so in other parts of Africa. The statement that " wherever Europeans live in an area of endemic malaria it is clearly necessary to supplement all other prophylactic procedures by means of chemoprophylaxis" would probably now be accepted by only a minority of tropical workers.

P. C. C. Garnham

Printed under the authority of His Majesty's Stationery Office
by the South Essex Recorders, Ltd., Ilford.

(1305) Wt. P11/325 3/48 S.E.R. Ltd. Gp. 432

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